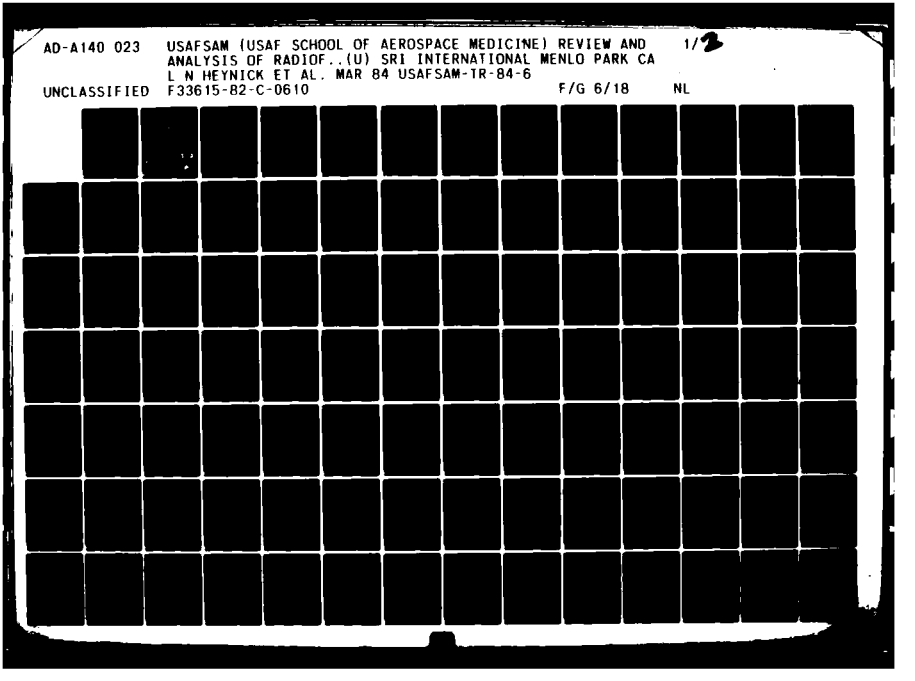
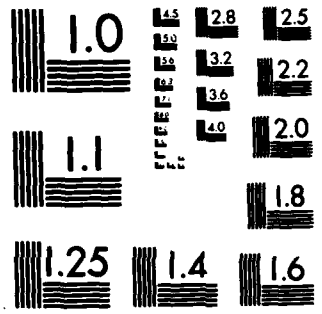
AD-A140 023 USAFSAM (USAF SCHOOL OF AEROSPACE MEDICINE) REVIEW AND 1/2
ANALYSIS OF RADIOF..(U) SRI INTERNATIONAL MENLO PARK CA
L N HEYNICK ET AL. MAR 84 USAFSAM-TR-84-6
UNCLASSIFIED F33615-82-C-0610 F/G 6/18 NL





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

AD A140023

Report USAFSAM-TR-84-6

12

USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: THIRD REPORT

Louis N. Heynick, M.S.
Peter Polson, Ph.D.

SRI International
333 Ravenswood Avenue
Menlo Park, California 94025

DTIC FILE COPY

DTIC
ELECTE
S APR 11 1984 D
D

March 1984

Interim Report for Period 17 May 1982 - 16 June 1983

Approved for public release; distribution unlimited.

Prepared for
USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas 78235

84 04 11 008

NOTICES

This interim report was submitted by SRI International, 333 Ravenswood Avenue, Menlo Park, California, under contract F33615-82-C-0610, job order 7757-01-87, with the USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas. James H. Merritt (USAFSAM/RZP) was the Laboratory Project Scientist-in-Charge.

When Government drawings, specifications, or other data are used for any purpose other than in connection with a definitely Government-related procurement, the United States Government incurs no responsibility or any obligation whatsoever. The fact that the Government may have formulated or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication, or otherwise in any manner construed, as licensing the holder, or any other person or corporation; or as conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

The Office of Public Affairs has reviewed this report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

James H. Merritt
JAMES H. MERRITT, B.S.
Project Scientist

John C Mitchell
JOHN C. MITCHELL, B.S.
Supervisor

Royce Moser
ROYCE MOSER, Jr.
Colonel, USAF, MC
Commander

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION: UNCLASSIFIED	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited.
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S): SRI Project 4472	5. MONITORING ORGANIZATION REPORT NUMBER(S): USAFSAM-TR-84-6
6a. NAME OF PERFORMING ORGANIZATION: SRI International; 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION: USAF School of Aerospace Medicine
6c. ADDRESS (City, State and ZIP Code): 333 Ravenswood Avenue, Menlo Park, California 94025	7b. ADDRESS (City, State and ZIP Code): Aerospace Medical Division (AFSC), Brooks Air Force Base, Texas 78235
8a. NAME OF FUNDING/SPONSORING ORGANIZATION; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: F33615-82-C-0610
8c. ADDRESS (City, State and ZIP Code)	10. SOURCE OF FUNDING NOS.

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT NO.
62202F	7757	01	87

11. TITLE (Include Security Classification): USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: THIRD REPORT

12. PERSONAL AUTHOR(S): Heynick, Louis N., and Polson, Peter

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Yr., Mo., Day)	15. PAGE COUNT
Interim Report	FROM 5/17/82 TO 6/16/83	1984 March	180

16. SUPPLEMENTARY NOTATION

17. COSATI CODES		
FIELD	GROUP	SUB. GR.
06	18	

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number): Nonionizing electromagnetic radiation; Radiofrequency radiation; Microwaves; and Biological effects.

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

The objectives of this project are to acquire, review, and analyze, on an ongoing basis, information on research pertaining to the biological effects of radiofrequency radiation (RFR) for the preparation of a computer data base of analyses at the USAF School of Aerospace Medicine (USAFSAM). The method in use is to: (1) select documents judged to be representative of prior and current research on various RFR-bioeffects topics, (2) analyze in detail the contents of each such document, and (3) assess the validity and significance of the results presented.

In this third report, the major RFR-bioeffects topics are listed and the revised format used for analyzing each selected document is described. During the period covered by this report, 38 additional analyses were completed, for a total of 118 analyses. The texts of the additional analyses are presented in Appendix A. Since the issuance of the first two reports, the analyses contained therein have been assigned identification numbers 1 through 80, and the sequence is continued for the analyses in Appendix A. In addition,

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS ☐	UNCLASSIFIED

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE NUMBER (Include Area Code)	22c. OFFICE SYMBOL
James H. Merritt, B.S.	(512) 536-3583	USAFSAM/RZP

DD FORM 1473, 83 APR — EDITION OF 1 JAN 73 IS OBSOLETE.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

19. ABSTRACT (Continued)
to the text, each analysis includes information for computer retrieval by authors, key words, year of publication, and RFR parameters. A master citation list of all 118 analyses completed thus far is given in Appendix B. This list is arranged alphabetically by first author.

CONTENTS

	Page
INTRODUCTION	3
METHODOLOGY	3
PROGRESS DURING THIS PERIOD	8
PROPOSED PLANS FOR THE FUTURE	9
ACKNOWLEDGMENT	9
APPENDIX A: TEXTS OF ANALYSES COMPLETED DURING THE THIRD PERIOD	11
APPENDIX B: MASTER LIST OF ANALYSES	165

FIGURES

Figure

1	Outline Form for Analyses	4
2	Type of Study	5
3	List of Key Words	7

Accession For
NTIS GRA&I ☒
DTIC TAB ☐
Unannounced ☐
Justification
By
Distribution/
Availability Codes
Dist | Avail and/or Special
A/1

USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: THIRD REPORT

INTRODUCTION

The objectives of this project are to acquire, review, and analyze, on an ongoing basis, information on research pertaining to the biological effects of radiofrequency radiation (RFR), and to provide periodic technical reports of our findings and assessments to the USAF School of Aerospace Medicine (USAFSAM) in specified formats.

The first technical report was for the period from 1 March through 31 August 1980 and was issued as Report SAM-TR-81-24 (November 1981). The second technical report was for the period from 1 September 1980 through 30 June 1981 and was issued as Report SAM-TR-82-16 (May 1982). The work culminating in these two reports was conducted on Contract Number F33615-80-C-0608 (SRI Project 1485). The present (third) report is for the period from 17 May 1982 through 16 June 1983; the work is being performed on Contract Number F33615-82-C-0610 (SRI Project 4472).

METHODOLOGY

Thousands of scientific papers, reports, books, summaries, and abstracts (referred to collectively herein as "documents") have been published on the bioeffects of RFR and related fields. Because references to most of these documents are readily available through various abstracting services and data bases, we are endeavoring to avoid needless duplication of such services and information. Instead, we are selecting documents judged to be representative of prior and current research on various RFR-bioeffects topics, analyzing the contents of each such document in detail, and assessing the validity and the significance of the results presented.

A major aspect of the project is to prepare the analysis of each selected document in a format that permits easy storage of the information in a computer at USAFSAM and retrieval by any of a variety of designators: analysis number, major bioeffects topic, author(s), year of publication, frequency, power density, modulation, duty cycle, specific absorption rate (SAR), species, and a list of special key words. The software for such retrieval is being developed by USAFSAM.

The analyses in the first two technical reports were printed with an optical-character-recognition (OCR-B) font, to permit direct storage of the information without retyping. This practice was found to be unsatisfactory and essentially redundant, and has been discontinued for the present report. In addition, the analysis format has been modified to conform with USAFSAM's retrieval software. The new outline form for analyses is displayed in Figure 1.

PRECEDING PAGE BLANK-NOT FILMED

Analysis number
Authors
Title
Citation

*

Author abstract (or reviewer summary)

**

Study type (bioeffects topic; in vivo/in vitro; species)
Effect type
Frequency
Modulation
Power density
SAR

Exposure conditions

Other information

Critique

References

***

[Retrieval information (one entry per line):]
Authors (last names only)

/

Key words

//

Year of publication
Frequency--value or range in MHz (0=unknown)
Duty cycle--value or range (CW=1; 0=unknown)
Power density--average value or range in mW/sq cm (0=unknown)
SAR--average value or range in W/kg (0=unknown)

///

Figure 1. Outline form for analyses.

To conform with the modified format, numbers 1 through 80 have been assigned serially to the analyses in the first two reports, and the sequence is continued in the present report. Inclusion of International Standard Serial Numbers (ISSNs) in the citations has been discontinued. The authors, title (in upper case), and reference are given immediately after the analysis number. The single asterisk after the citation is a flag to permit retrieval of only the citation part of the analysis, if desired.

As part of each analysis, the abstract or summary provided by the authors is reproduced without comment directly after the citation (a change from the previous outline) and the heading "AUTHOR ABSTRACT" or "AUTHOR SUMMARY" is used. If the document does not contain an abstract or summary, its important contents are summarized without comment, and the heading "REVIEWER SUMMARY" is used to indicate this fact. The two asterisks following the abstract or summary comprise a flag to permit retrieval of only the citation and abstract or summary, if desired.

Next, for each document reviewed, one or more pertinent major topics are listed under "Study type." To conform better with current usage, the list of topics used in the previous reports has been modified. The new list is shown in Figure 2. Because numerical designators for each topic are not necessary as retrieval information, they are no longer used. Also indicated under this heading are whether the study was done in vivo or in vitro and the species involved.

Auditory Effects
Behavior
Biorhythms
Cardiovascular Effects
Cellular and Subcellular Effects
Endocrinology
Environmental Factors
Exposure Methods, Dosimetry, and Modeling
Human Studies
Immunology and Hematology
Mechanisms of Interaction
Medical Applications
Metabolism and Thermoregulation
Multiagent Interactions
Mutagenesis, Carcinogenesis, and Cytogenetic Effects
Nervous System
Ocular Effects
Physiology and Biochemistry
Teratology and Developmental Abnormalities

Figure 2. Type of study.

Under the heading "Effect type," the specific effects, phenomena, biological endpoints, or other characteristics sought or studied are listed briefly. The frequencies, modulation (continuous wave (CW), amplitude-modulation, or pulse parameters), power densities, and SARs are given under their respective headings.

In the next section, "EXPOSURE CONDITIONS," the salient features of the exposure arrangements and parameters are briefly summarized.

Under "OTHER INFORMATION," any important information in the text of the document that was not included in the author abstract or summary or that is not appropriate for the reviewer summary is summarized , again without comment.

Our analysis of the document is given under "CRITIQUE." To the extent possible or appropriate, each critique includes evaluation of the data presented (including the statistical aspects if the data presented are adequate), the biological and engineering methodology used, the validity of the results, how the findings compare with those of other investigations, and the significance of the findings with respect to the health of humans (and/or other species) exposed to RFR. It should be noted that critiques are no longer labeled "INITIAL" or "FINAL," with the view that any critique should be subject to possible revision, e.g., updates in the light of subsequent information or comments from the authors. With regard to the latter point, the inclusion of written comments offered by authors or others is planned as addenda to the critique.

Any literature citations mentioned in the analysis are shown under "REFERENCES." The three asterisks after the references section mark the end of the analysis proper and comprise a flag to permit retrieval of the full text of the analysis proper.

The following items are solely for retrieval of the analysis by any of various designators. Listed first are the last names individually of all the authors of the document, followed by a single slant sign (/) to indicate the end of this form of designator. The next set of designators are key words derived from the analysis of the document. Such key words are not necessarily those provided by the authors, but are from a list being designed expressly for USAFSAM retrieval use. The current list is displayed in Figure 3. Additions to the list may be made as appropriate. This designator section is terminated with two slant lines (//).

ANTIGEN
ANTIBODY
AUDITORY
BACTERIA
BEHAVIOR
BIOCHEMISTRY
BIORHYTHM
BBB
BRAIN-UPTAKE-INDEX
CALCIUM
CARCINOGENIC
CARDIOVASCULAR
CAT
CELLULAR
CHICKEN
CHINCHILLA
CHRONIC
CIRCADIAN
COMPLEMENT
CORTICOSTEROID
CW
CYTOGENETIC
DEVELOPMENT
DIELECTRIC
DOG
DOSIMETRY
DROSOPHILA
DRUG-RFR
E-COLI
ECOLOGICAL
EEG
EFFLUX
EMBRYO
ENDOCRINOLOGIC
ENVIRONMENTAL
EPIDEMIOLOGIC
ESTRUS
EVOKED-POTENTIAL
EXPOSURE-SYSTEM
GUINEA-PIG
HAMSTER
HAPLOTYPE
HEMATOLOGY
HISTOLOGY
HUMAN
HYPERTHERMIA
HYPOTHERMIA
IMMUNOLOGY
INFLAMMATION
INSTRUMENTATION
IN-VITRO
IN-VIVO
LETHALITY
LEUKOCYTE
LYMPHOCYTE
MECHANISMS
MEDICAL
METABOLISM
MICROSCOPY
MITOGEN
MODEL
MODULATED
MONKEY
MORBIDITY
MORTALITY
MOUSE
MULTIAGENT
MUTAGENIC
NERVOUS-SYSTEM
OCCUPATIONAL
OCULAR
PHYSIOLOGY
POSITIVE-CONTROL
PRIMATE
PULSED
QUAIL
RABBIT
RAT
RECTAL
REPEATED-ACQUISITION
REVIEW
RFR
STRESS
TENEBRIO
TERATOGENIC
THERMOREGULATION
THRESHOLD
TRACER
WEIGHT
YEAST

Figure 3. List of key words.

In the final section of designators, the following numerical information is presented in sequence: the year of publication of the document; the frequency or frequency range of the RFR in MHz; the duty cycle or range thereof, with "1" representing continuous-wave (CW) RFR; the average power density or its range; and the average SAR or its range. Where appropriate, the duty cycles and average power densities can be used to calculate peak power densities. The symbol "0" is used to signify "unknown" or "not specified". This designator section is terminated with three slant lines (///), which also indicate the end of the entire analysis, including the retrieval information.

The analyses in Appendix A illustrate this methodology.

PROGRESS DURING THIS PERIOD

By the end of this period, 38 additional analyses were completed, for a total of 118 in the three reports. The texts of the 38 analyses (inclusive of the retrieval data) are presented in sequence by citation number in Appendix A.

A master list of reference citations for all of the 118 analyses completed thus far is presented in Appendix B. This list is in alphabetical order by first author. For ease in finding the text of any analysis, the three reports are referred to by Roman numerals in chronological succession, and the end of each reference citation in the master list is annotated with the Roman numeral of the report containing the text of the analysis, followed by the first page number of the text. This annotation method is illustrated below:

62
Adair, E.R. and B.W. Adams
MICROWAVES MODIFY THERMOREGULATORY BEHAVIOR IN SQUIRREL MONKEY
Bioelectromagnetics, Vol. 1, No. 1, pp. 1-20 (1980) (II-72)

The annotation "II-72" indicates that this analysis can be found on page 72 of the second report.

Initially, it was intended that collective summaries be prepared of the current state of knowledge of each major topic, based on the analyses completed on that topic. (This task was done for "Epidemiologic," and the collective summary of the initial set of analyses under that topic was included in Report I.) However, it was subsequently realized that a periodic summary of a topic based solely on the analyses completed on any given date on that topic could constitute an unbalanced account of the overall status of that topic, because important documents not yet fully

analyzed may not have been included. Moreover, under other projects, SRI has prepared what are believed to be balanced accounts of the then-current status of each topic in connection with Environmental Impact Statements or Assessments for several proposed RFR-emitting systems. The latest review of this kind is "Bioeffects of Radiofrequency Radiation: A Review Pertinent to Air Force Operations," by L.N. Heynick and P. Polson, issued as USAFSAM Report SAM-TR-83-1 (March 1983). Accordingly, no topic summaries are included in the present report. However, topic summaries and/or updates of the cited review are planned as appropriate and will be issued in the future.

PROPOSED PLANS FOR THE FUTURE

It is proposed to continue performing detailed analyses of important documents on biological effects of RFR to augment the data base produced thus far under this project.

ACKNOWLEDGMENT

The contributions of Jane M. Clemmensen, Research Engineer, to this report and the guidance furnished by Jacqueline Bremer, Administrative Assistant, in the techniques of word processing are appreciated very much.

APPENDIX A

TEXTS OF ANALYSES COMPLETED DURING THE THIRD PERIOD

PRECEDING PAGE BLANK-NOT FILMED

81
Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982)

*

AUTHOR ABSTRACT: Time-bred CD-1 mice (100) were sham-irradiated or irradiated with 2450-MHz (CW) microwaves at 28 mW/sq cm for 100 minutes daily from the 6th through 17th day of gestation. The offspring were examined either as fetuses after hysterotomy on the 18th day of gestation or as naturally born neonates on the 1st and 7th day of age. Fetuses of half of the dams were examined on the 18th day of gestation.

The incidence of pregnancy and the numbers of live, dead, resorbed, and total fetuses were similar in both groups. The mean weight was significantly lower (10%) in live microwave-irradiated fetuses, and ossification of sternal centers was significantly delayed. In the offspring that were born naturally, the mean weight of microwave-irradiated 7-day-old suckling mice was significantly lower (10%) than that of the sham-irradiated group. Survival rates of neonates in these two groups were not different. These data demonstrate that the decreased fetal weight seen in microwave-irradiated mice is retained at least 7 days after birth. Evidence from other published studies is presented to show that the retarded growth is persistent and might be interpreted as permanent stunting.

**

Study Type: Teratology and Developmental Abnormalities, Physiology and Biochemistry; IN VIVO; MOUSE
Effect Type: RFR-induced fetal abnormalities and weight deficits in fetuses and pups
Frequency: 2.45 GHz
Modulation: CW
Power Density: 28 mW/sq cm
SAR: 16.5 W/kg array mean; 4.5 W/kg standard deviation

EXPOSURE CONDITIONS: Two 5x5 arrays of pregnant mice in individual vented plastic cages were exposed to far-field RFR for 100 min/day from gestational days 6 through 17 in an anechoic chamber at 20.2 deg C ambient temperature and 50% relative humidity. Two other arrays were similarly sham-exposed.

OTHER INFORMATION: The exposure conditions were essentially the same as those described in Berman et al. (1978) for 5x5 arrays of mice, so the SAR at 28 mW/sq cm varied with position from about 11.3 to 20.6 W/kg. Two replicate experiments were performed, each involving 25 RFR-exposed and 25 sham-exposed mice. In the first replicate, 12 RFR-exposed mice in alternate positions in the array and 12 sham-exposed mice in the same positions were allowed to come to term; the uteri of the other 13 mice

PRECEDING PAGE BLANK-NOT FILMED

in each group (including those in the 25th position) were examined on gestational day 18. The mice in the second replicate were treated in the same manner except for those in the 25th position, which were allowed to come to term. The resorptions and live and dead fetuses taken on day 18 were counted. The live fetuses were weighed individually, fixed, macerated, and cleared, and their sternal ossification centers were examined. For the mice that came to term, the live and dead neonates were counted on the morning after birth and at age 7 days, at which time the live offspring of each litter were weighed as a group. Only the data on litters born on gestational day 20 were reported.

No statistically significant differences between RFR- and sham-exposed groups were found in numbers of live or dead fetuses or litter sizes. For the RFR-exposed mice, the numbers of pups born alive or still alive at 7 days were both larger than for the sham-exposed mice, and the numbers of stillborn or of pups that died since birth were both smaller for the RFR-exposed than the sham-exposed mice. However, none of these results was statistically significant. Also, all of the fetuses were apparently normal; no gross morphologic anomalies were seen. Some of the fetuses were visibly small for their gestational age, but this condition by itself is not considered a valid example of frank terata.

The progression of appearance and number of sternal ossification centers in a fetus is an indication of skeletal developmental stage. The number of such centers in each live fetus on gestational day 18 was determined. The mean number per fetus for the RFR-exposed group was smaller than for the sham-exposed group, but the difference was barely significant ($p=0.049$).

The mean of the litter-average live-fetal weights (on gestational day 18) for the RFR-exposed group was about 10% smaller than for the sham-exposed group; the difference was significant at the $p<0.01$ level (analysis of variance). The mean litter-average pup weight at age 7 days was also about 10% smaller ($p<0.05$) for the RFR-exposed group than for the sham-exposed group. Because the variances of mean pup weights were much larger than the variances of mean fetal weights, the investigators did a log-transformation of the weight data and treated the transformed data by an analysis of covariance for a two-way design. The results showed that the number of live offspring was a significant source of variation, and that large litters had small litter mean weights per fetus or offspring and vice versa.

The authors listed and compared their results with those of other investigators of weight alterations in pre- and postnatal mice induced by RFR (mostly at 2.45 GHz) at various power densities and corresponding SARs. Most of these investigators reported significantly smaller weights for RFR-exposed than control mice at 10 mW/sq cm or higher, or SARs of 3 W/kg or higher. The only investigation at lower values in the list was by Berman et al. (1978), in which a nonsignificant weight increase was found for exposure at 3.4 mW/sq cm or an SAR of 2 W/kg.

CRITIQUE: As in Berman et al. (1978), the large positional variations of whole-body SAR may be an indication of mutual RFR interactions among the mice.

Two replicate experiments were performed, involving totals of 50 RFR-exposed and 50 sham-exposed pregnant mice. Apparently the results of the two experiments were combined, but it would have been interesting to note whether there were any significant differences in results between them. Also, for unstated reasons, the results presented are for fewer than the numbers of animals involved.

The results of this investigation support the findings of Berman et al. (1978) that exposure of pregnant mice to 2.45-GHz RFR at 28 mW/sq cm yields about 10% smaller mean weights of live fetuses and neonates than the values for sham-exposed mice. However, in contrast with the previous investigation no morphologic abnormalities were found in the live fetuses or pups. Thus, the smaller fetal and pup weights were the only significant effects possibly ascribable to RFR. Because the exposure conditions used were the same as those in the previous investigation, in which a slight increase in rectal temperature was reported, these weight deficits appear to have been thermally induced. This interpretation is supported by the results of Inouye et al. (1982) and Nawrot et al. (1981), who demonstrated that exposure of pregnant mice to elevated ambient temperatures (without RFR) can be teratogenic.

REFERENCES:

Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978)

Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982)

Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)

***

BERMAN
CARTER
HOUSE

/

BIOCHEMISTRY
CW
DEVELOPMENT
EMBRYO
IN-VIVO
MOUSE
RFR
TERATOGENIC
WEIGHT

//

1982
2450
1
28
16.5

///

82
Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915 MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b)

*

AUTHOR ABSTRACT: Thirty pregnant Wistar strain albino rats were used to determine the effects of chronic prenatal exposure to 915 MHz microwave radiation at a continuous wave power density level of 10 mW/sq cm on postnatal growth and neurobehavioral development. Eleven rats were irradiated in a fully characterized anechoic chamber from days 1 to 21 of gestation. Mean total exposure time was 6544 min. Nineteen rats were used as control animals. All animals delivered and raised their offspring (F1a) until weaning at 30 days of age. Ten days later females were rebred and a standard teratologic evaluation was completed on the resultant F1b fetuses. Maternal brain, liver, kidneys, and ovaries were removed, weighed, examined, and fixed in formalin. The F1a (irradiated) neonates were given four perinatal reflex tests (surface righting, air righting, auditory startle, visual placing). One physiological parameter, eye opening, was also observed. Weekly weights were recorded throughout the study period. At 60 days of age the offspring were randomly given 3 of 6 tests (conditioned avoidance response, water T-maze, open field, activity wheel, forelimb hanging, swimming). At 90 days of age reproductive capability was evaluated and a standard teratologic analysis performed on the resultant F2 offspring. The brain, liver, kidneys, and gonads of all F1a offspring were removed, weighed, examined, and fixed in formalin. No significant morphologic or neurobehavioral alterations were observed due to chronic prenatal exposure to 915 MHz microwave radiation at a continuous wave power density level of 10 mW/sq cm.

**

Study Type: Teratology and Developmental Abnormalities, Behavior; IN VIVO; RAT
Effect Type: Effects of prenatal RFR exposure on postnatal growth and neurobehavioral development
Frequency: 915 MHz
Modulation: CW (amplitude modulated)
Power Density: 10 mW/sq cm
SAR: About 4 W/kg

EXPOSURE CONDITIONS: Groups of up to 4 pregnant rats (11 rats total) were isolated from one another in Acrylite cages and exposed at 10 mW/sq cm for 6 hr/day without food or water in an anechoic chamber during gestational days 1 to 21. To minimize orientation-dependent SAR variations, the antenna was rotated at 30 rpm (which probably introduced a small percentage of amplitude modulation). A group of 4 rats denoted as "concurrent controls" were similarly sham-exposed.

OTHER INFORMATION: RFR exposures were for 6 hr/day at 10 mW/sq cm throughout gestation. Using the mean maternal body weight for the gestational period, the investigators derived a mean SAR of about 4 W/kg. In a parallel study (Jensh et al., 1982a) involving similar exposure conditions, prenatal effects were sought. As in that study, in addition to the 11 RFR-exposed ("experimental") rats and the 4 sham-exposed ("concurrent-control") rats, 5 rats kept in home cages (the "HC" group) and 10 rats kept daily for 6 hr in the anechoic chamber (the "AC" group) presumably with the exposure apparatus entirely off, served as two "baseline-control" groups. After delivery of these initial litters (F1a offspring), neonatal weights were recorded weekly until age 87 days. These neonates were given four reflex tests starting on the indicated postnatal day. The expected mean age for achieving criterion performance, based on results for 30 colony-control litters, is also indicated. The tests were: surface righting (day 3, criterion age 9.2 days), air righting (day 14, criterion age 14.0 days), and visual placing (day 16, criterion age 23.7 days). The age for eye opening was also sought, starting on day 12. These neonates were weaned on day 30. At age 60 days, they were given either a conditioned avoidance response (shuttle-box) test or a water T-maze test and two of the following four tests: open field, 24-hr activity wheel, forelimb hanging, swimming. At 90 days of age, half the F1a offspring were killed and examined for histopathology. The remaining offspring were bred in four groups: control male to control female, control male to experimental female, experimental male to control female, and experimental male to experimental female. The resulting litters (F2) were examined prenatally for teratogenesis. Also, the original females were rebred 40 days after delivery of the F1a offspring (but not reexposed to RFR) and the resulting fetuses (F1b) were examined for teratogenesis.

The results for the initial pregnancy showed no significant differences in maternal weight, weight gain, or F1a mean litter size. Only one abnormal neonate, in the baseline AC group, was found. The mean weekly weights of the RFR-exposed F1a neonates were significantly larger than for the concurrent-control neonates through age 24 days, after which the differences were statistically nonsignificant. There were also some significant weight differences, at various ages, among the baseline (HC and AC) groups and the concurrent control group. In all four reflex tests, the RFR exposed F1a neonates achieved criterion performance significantly sooner than the concurrent controls. However, there was no significant difference in mean age of eye opening. The behavioral tests at age 60 days yielded no significant differences among the four groups. Necropsies of the F1a offspring at 90 days showed no significant differences between the RFR-exposed and concurrent-control groups in organ weights or organ/body weight ratios.

For the second breeding of the original females, there were no significant differences between the RFR- and concurrent-control groups in maternal weight or mean litter size, and no abnormal offspring were evident. Also, subsequent necropsies of these mothers showed no significant differences in mean organ weights or organ/body weight ratios.

In the cross breeding of F1a males and females to obtain F2 fetuses, there were no significant RFR-related differences in maternal weight, percentage of resorptions, fetal weight, or litter size.

CRITIQUE: As in the parallel investigation (Jensh et al., 1982a), the differences in treatment between the baseline-AC and the concurrent-control (sham-exposed) groups are not clear. Significant differences between these control groups were found for several of the endpoints studied, indicating the presence of non-RFR factors. Thus, in seeking possible RFR-induced bioeffects, only the comparisons between the RFR-exposed and sham-exposed groups appear pertinent.

There are several minor discrepancies between statements in the text regarding statistical significance of the results and calculations for the corresponding mean data. Most of these discrepancies appear in the differences among the three control groups and therefore are of peripheral relevance. However, the investigators state (p. 78) that "there was a slight, but statistically significant ($p<0.05$) decrease in mean litter size among the mothers previously exposed to irradiation when compared to concurrent control mothers." Calculation of t from the mean data and standard deviations presented in their Table 6 yields a value of 1.64, which, for 12 degrees of freedom, corresponds to $p>0.05$ (nonsignificant difference) in either the 2-tailed or 1-tailed test.

In their summary, the investigators concluded that "chronic prenatal exposure of rats to 915 MHz microwave radiation at a power density level of 10 mW/sq cm did not result in significant postnatal neurobehavioral modifications or in significant alterations in growth and development." These findings are consonant with those of Chernovetz et al. (1977) and Berman et al. (1981) with rats. However, one minor effect noted by Jensh et al. was that the perinatal mean weekly weights of the RFR-exposed F1a neonates were significantly larger than for the concurrent controls. This effect is opposite to that found by Berman et al. (1982) in mice exposed to 2.45-GHz RFR at 28 mW/sq cm (SAR 16.5 W/kg). The other minor effect found by Jensh et al. was the earlier achievement of criterion performance in the reflex tests by the RFR-exposed rats. Both of these effects appear to indicate that prenatal exposure to relatively low levels of RFR may be beneficial, but such findings should be subject to independent experimental verification.

REFERENCES:

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981)

Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982)

Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977)

Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a)

***

JENSH
VOGEL
BRENT

/

BEHAVIOR
CW
DEVELOPMENT
HISTOLOGY
IN-VIVO
MODULATED
NERVOUS-SYSTEM
RAT
RFR
TERATOGENIC
WEIGHT

//

1982
915
1
10
4

///

83
Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a)

*

AUTHOR ABSTRACT: Thirty-nine pregnant Wistar strain albino rats were used to determine possible teratogenic activity due to chronic exposure with microwave radiation at a field intensity of a 10 mW/sq cm at a frequency of 915-MHz microwave radiation. Ten rats were irradiated in a fully characterized anechoic chamber from Days 1 to 21 of gestation. The results of preliminary studies using 20 pregnant rats indicated that this power density was the maximal level which did not cause increased rectal temperature. Twenty-nine pregnant females were used as control animals. On the 22nd day of gestation animals were killed and maternal brain, liver, kidneys, and ovaries were removed, examined, weighed, and fixed in buffered formalin. Fetuses and placentae were removed, examined, weighed, and fixed in Bouin's fixative. All fetuses were examined for malformations using a cross-section dissection methodology.

No significant alterations were observed for the following parameters: maternal body weight and weight gain, term maternal organ weight and organ/body weight ratios, resorption rate, abnormality rate, mean litter size, or mean term fetal weight. No significant teratogenic activity was observed, using these criteria, due to chronic exposure of pregnant rats to 915-MHz continuous wave microwave radiation at a 10 mW/sq cm power density.

**

Study Type: Teratology and Developmental Abnormalities;
IN VIVO; RAT
Effect Type: RFR-induced alterations of maternal organ weight and effects on fetal resorption and abnormality rates, litter size, and fetal weight
Frequency: 915 MHz
Modulation: CW (amplitude modulated)
Power Density: 10 mW/sq cm
SAR: 3.57 W/kg

EXPOSURE CONDITIONS: Six groups of up to 4 pregnant rats were isolated from one another in Acrylite cages and exposed at 10 mW/sq cm for 6 hr/day without food and water in an anechoic chamber during gestational days 1 to 21. To minimize orientation-dependent SAR variations, the antenna was rotated at 30 rpm (which probably introduced a small percentage of amplitude modulation). Two groups of rats denoted as "concurrent controls" were similarly sham-exposed.

OTHER INFORMATION: In the first of two preliminary experiments, pregnant rats were exposed for 6 hr at 25 mW/sq cm or incrementally lower values, and their rectal temperatures were measured prior to, during, and up to 90 min after exposure. No statistically significant temperature increases were observed at 11.6 mW/sq cm or lower. In the second experiment, 6 rats on gestational day 1 and 14 rats on day 20 were similarly treated at about 11.6 mW/sq cm. For both groups, the mean 90-min post-exposure temperature was significantly lower than the pre-RFR and mid-RFR values. In addition, although the investigators state otherwise, the data show that for the group exposed on day 20, the mid-RFR temperature was significantly higher than the pre-exposure value. The results of these experiments served as the basis for using 10 mW/sq cm in this investigation. The mean maternal body weight for the gestational period was 0.28 kg, from which the investigators derived a mean SAR of 3.57 W/kg at 10 mW/sq cm. For this investigation, 11 pregnant rats exposed to the RFR comprised the "experimental" group and 4 sham-exposed rats comprised the "concurrent control" group. Fifteen other pregnant rats were concurrently RFR- or sham-exposed for postnatal functional analysis (Jensh et al., 1982b). In addition, 5 rats kept in home cages (the HC group) and 10 rats kept daily for 6 hr in the anechoic chamber (the AC group) presumably with the exposure apparatus completely off, served as two "baseline control" groups.

The rats were euthanized on gestational day 22. Weights of maternal brain, liver, kidneys, and ovaries were measured and normalized to term body weights. No statistically significant differences in organ-to-body weight ratios were found between the HC and AC baseline control groups or between the experimental and concurrent control groups for any of the organs. However, significant differences were found between the baseline control groups and the concurrent control group, results ascribed to the significantly lower mean body weights of the baseline groups, which consisted of younger animals than those of the experimental and concurrent control groups. The unnormalized mean organ weights showed no significant differences among the four groups.

There were no statistically significant differences in mean litter size or mean 21-day-old fetal weight among the four groups. Only one fetus, in the AC baseline group, was abnormal. Resorption rates for these two baseline groups were not included, but were found to be 7.1% and 12% for comparable HC and AC baseline groups, respectively. The resorption rate for the RFR-exposed group was 4.4%. In the concurrent control group, an entire litter of 13 fetuses was resorbed by one of the rats; inclusion of these resorptions yielded a rate of 25.5%.

CRITIQUE: The measures taken by these investigators to obtain uniform exposures were excellent. Not clear are the differences in treatment between the baseline-AC and the concurrent-control (sham-exposed) groups. Also, the fact that the mean body weights for these two groups differed significantly tends to confound comparisons between them of the various biological endpoints studied. Thus, in seeking possible RFR-induced bioeffects, only the comparisons between the RFR-exposed and sham-exposed groups appear pertinent. The results for these two groups

showed no statistically significant differences for any of the biological endpoints measured. The 10 mW/sq cm power density was used with the implication that no significant increase in rectal temperature would occur because none was seen at about 11.6 mW/sq cm. However, the results for their second preliminary experiment on gestational day 20 did show a significant (t=2.24) temperature increase during exposure. Moreover, the significant post-exposure drop in temperature in both the gestational-day-20 and day-1 rats indicates that the rats were being thermally stressed. Thus, these negative findings are consonant with those of other investigations with rats, notably the studies of Chernovetz et al. (1977) and Berman et al. (1981), conducted at 2.45 GHz, which showed that much higher SARs are necessary for teratogenic effects in rats.

REFERENCES:

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981)

Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977)

Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915 MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b)

***

JENSH
WEINBERG
BRENT

/

CW
DEVELOPMENT
EMBRYO
HISTOLOGY
IN-VIVO
MODULATED
RAT
RFR
TERATOGENIC
WEIGHT

//

1982
915
1
10
3.57

///

84
Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981)

*

AUTHOR ABSTRACT: Female Sprague-Dawley (CD) rats were exposed to 2450-MHz (CW) microwave radiation at incident power densities of 0 or 28 mW/sq cm for 100 min daily on the 6th through 15th day of gestation. The whole-body specific absorption rate at 28 mW/sq cm is estimated to be 4.2 W/kg. These exposure conditions raised rats' average colonic temperatures to 40.3 deg C at the end of irradiation. There were 67 sham-irradiated and 70 microwave-irradiated females. When these groups were compared, no significant differences were found in pregnancy rates; in the numbers of live, dead, or total fetuses; in the incidences of external, visceral, or skeletal anomalies or variations; or in the body weight of live fetuses. It is concluded that these conditions do not have an effect on the gross structure of the fetal rat when applied repetitively during post-implantation pregnancy. It is also strongly suspected that this lack of an effect may hold true at any exposure level less than that which will kill a significant number of the dams by hyperthermia (colonic temperature >40 deg C).

**

Study Type: Teratology and Developmental Abnormalities;
IN VIVO; RAT
Effect Type: RFR-induced effects on pregnancy rates, numbers of live and dead fetuses, and incidences of fetal anomalies
Frequency: 2.45 GHz
Modulation: CW
Power Density: 28 mW/sq cm
SAR: 4.2 W/kg

EXPOSURE CONDITIONS: Groups of 8 time-bred rats in individual Plexiglas containers were arranged in 3x3 rectangular arrays with central position unoccupied and the long axis of each container parallel to the H-vector and perpendicular to the propagation direction. Each array was sham-exposed or exposed to far-field 2.45-GHz RFR at 28 mW/sq cm for 100 min/day on gestational days 6 through 15 at 22.2 deg C ambient temperature and 50% relative humidity.

OTHER INFORMATION: Each rat was euthanized on gestational day 21, and the live, dead, and resorbed conceptuses were counted. Each live fetus was dried, examined for external morphology, weighed, fixed, and subsequently studied for internal morphology. There were no statistically significant differences between RFR- and sham-exposed rats in pregnancy rates; mean litter values of live, dead, resorbed, or total fetuses; or live fetal weight. The numbers of ribs and sternal ossification centers were comparable. The types and indices of major

and minor terata were similar in both groups of litters. No encephaloceles (brain hernias) were seen in any of these litters.

Regarding these negative results, the authors concluded that "the fetal rat appears to lack the capability to respond to radio-frequency radiation by a clear demonstration of effects at doses less than that which are lethal to a portion of the dams," and therefore that the rat is an inappropriate model for determining whether RFR would be teratogenic to humans in exposure situations not lethal for the mothers. They then suggested that the mouse fetus is a more appropriate model for assessing such human risk.

CRITIQUE: These negative results with the rat at a whole-body SAR of 4.2 W/kg (incident power density of 28 mW/sq cm at 2.45 GHz) are consonant with those of Chernovetz et al. (1977), who found no teratogenic effects from exposure to 2.45-GHz RFR at about 31 W/kg, which was lethal to about 27% of the dams. It is also noted that Jensh et al. (1982a, 1982b) obtained no teratogenic effects on the rat with an incident power density of 10 mW/sq cm at 915 MHz (calculated SAR of about 3.6 W/kg).

However, the point made by Berman et al. that the mouse may be a better model than the rat as a surrogate for humans in investigating RFR teratogenesis is open to question, especially for studies involving chronic, low-level exposures. Most of the recent results with mice indicate the existence of a threshold SAR (or power density) for teratogenesis, and the effects above the threshold were evidently due to the heat produced by the RFR. For example, Inouye et al. (1982) and Nawrot et al. (1981) found no teratogenic effects with 2.45-GHz RFR below about 40 W/kg (or 30 mW/sq cm), and the only significant effect found by Berman et al. (1982) on the mouse was lower fetal and neonatal weight for exposure at 16.5 W/kg (or 28 mW/sq cm). Because the thermoregulatory systems of both the rat and mouse are much less efficient than the human system, neither kind of rodent appears to be a satisfactory model for studying RFR-teratogenesis. Any of the nonhuman primates would be more suitable.

REFERENCES:

Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982)

Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977)

Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982)

Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a)

Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b)

Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)

***

BERMAN
CARTER
HOUSE

/

CW
DEVELOPMENT
EMBRYO
IN-VIVO
RAT
RFR
TERATOGENIC
WEIGHT

//

1981
2450
1
28
4.2

///

85
Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982)

*

AUTHOR ABSTRACT: The development of preimplantation embryos after exposure to microwave radiation was studied. Female CD-1 mice were induced to superovulate, mated, and exposed to 2.45-GHz microwave or sham radiation for 3 h at power densities of 9 mW/sq cm on either day 2 or 3 of pregnancy (plug day was considered day 1). Another group of mice was exposed to heat stress by placing the dams in an environmental room at an ambient temperature of 38 deg C and relative humidity at 62% for 3 h on day 2 of pregnancy. All groups were euthanized on day 4 of pregnancy and embryos were recovered by flushing excised uterine horns. Embryos were examined for abnormalities and classified by the developmental stages. They were then treated with hypotonic solution and dissociated for counting blastomeres. Heat stress caused stunted development of embryos, but no remarkable effect of microwave radiation could be found on the development of preimplantation embryos.

**

Study Type: Teratology and Developmental Abnormalities, Cellular and Subcellular Effects; IN VIVO; MOUSE
Effect Type: RFR- and temperature-induced effects on preimplantation embryos
Frequency: 2.45 GHz
Modulation: CW
Power Density: 9 or 19 mW/sq cm
SAR: 11.7 or 24.7 W/kg

EXPOSURE CONDITIONS: Four groups of pregnant mice in individual Styrofoam cages were exposed in circular arrays to far-field RFR in an anechoic chamber for 3 hr at either power density during gestational day 2 or 3 at 22 deg C ambient temperature and 60% relative humidity. Two groups were sham-exposed under the same conditions. One group was exposed to 38 deg C ambient temperature and 60% relative humidity without RFR.

OTHER INFORMATION: The power density at each location in the array was measured with an NBS probe with the mouse absent but with the mice present in the other locations. The mice were spaced at least 2 wavelengths apart, and no power density changes were detected at each location due to the presence or movement of the mice in the other locations. Spatial variations of power density over the circular array were about 10%. The SARs cited above were for mice curled up (asleep), the configuration taken during most of the exposure period.

No increase in colonic temperature was obtained at 9 mW/sq cm, 1 deg C increase occurred at 19 mW/sq cm, and at least 2.2 deg C occurred for the 38 deg C heat treatment. Prior to treatment, the mice were chemically induced to superovulate and were caged overnight in pairs with males. The next day was taken as gestational day 1. First cleavage of mouse embryos occurs about 24 hr after fertilization, second cleavage (to 4 cells) about 13 hr later (37 hr after fertilization), and third cleavage (to 8 cells) about 10 hr later. Thus, treatment on day 2 was during the 2-cell stage, and treatment on day 3 was during the 4- to 8-cell stages.

On day 4, embryos were counted, examined for abnormalities, and classified by developmental stage as: morula (9 or more blastomeres but no blastocoelic cavity), early blastocyst (small blastocoelic cavity), or blastocyst (large blastocoelic cavity). Abnormal embryos were defined as underdeveloped (less than 9 blastomeres) and as fragmented and/or collapsed embryos. There were no statistically significant differences in the number of fertilized mice, the number of embryos per mouse, or the percentage of abnormal embryos (total and per dam) among all the groups. In addition, there were no significant differences in embryonic development or in abnormal embryos between RFR-exposed groups (at either power density) and sham-exposed groups for either treatment day. However, the heat treatment caused stunted embryonic development, i.e., significant increases in the number of morulae and decreases in the numbers of blastocysts compared with numbers for sham-exposed mice on corresponding treatment days.

CRITIQUE: As an aside, the term "preimplantation embryo" used by these investigators is not strictly correct; the term "embryo" applies only after the long axis appears (Dorland, 1981).

Direct comparisons of the results of this investigation with those of Nawrot et al. (1981), performed in the same laboratory with the same mouse strain (CD-1), are difficult because in the latter investigation, the dams were exposed for 8 hr/day over gestational days 1-6 or 6-15 (in contrast with a single 3-hr exposure on day 2 or 3), and the fetuses were examined at a much later stage of gestation (day 18 versus day 4). Moreover, the frequent handling of the dams was a significant factor in the earlier investigation. Nevertheless, the negative results for RFR exposure at 9 and 19 mW/sq cm obtained by Inouye et al. (1982) are consonant with the approximately 30 mW/sq cm threshold found by Nawrot et al. (1981). In addition, fetal stunting occurred in both investigations from exposure of the dams to elevated ambient temperatures without RFR.

REFERENCES:
DORLAND'S ILLUSTRATED MEDICAL DICTIONARY
26th Ed., W.B. Saunders Co., Philadelphia, Pa., p. 432 (1981)

Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)

***

INOUYE
MATSUMOTO
GALVIN
MCREE

/

CELLULAR
CW
DEVELOPMENT
EMBRYO
HYPERTHERMIA
IN-VIVO
MOUSE
RFR
STRESS
TERATOGENIC

//

1982
2450
1
9-19
11.7-24.7

///

86
Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)

*

AUTHOR ABSTRACT: The embryofetal toxicity and teratogenicity of plane-wave 2.45 GHz continuous wave (CW) microwave radiation at different intensities were investigated in the CD-1 mouse. Mice were exposed on days 1-15 of gestation to an incident power density of 5 mW/sq cm (specific absorption rate of 6.7 mW/gm) and either on days 1-6 or 6-15 of gestation to 21 mW/sq cm (specific absorption rate of 28.14 mW/gm) or to 30 mW/sq cm (specific absorption rate of 40.2 mW/gm) for 8 hours daily. Exposure either on days 1-6 or 6-15 of gestation to a power density of 21 or 30 mW/sq cm caused an increase in colonic temperature of exposed dams of 1 deg C and 2.3 deg C, respectively.

To distinguish between "thermal" and "nonthermal" effects of 21 or 30 mW/sq cm, groups of mice were also exposed to elevated ambient temperature to raise their body temperature to the level of those animals exposed to microwave. Ambient temperatures of 30 deg C and 31 deg C increased the deep colonic temperature to that obtained with the 21 and 30 mW/sq cm microwave exposure, respectively. The temperature-exposed mice were handled in exactly the same manner as the microwave-exposed mice. A significant reduction in maternal weight gain, either during treatment on days 1-6 or 6-15 of gestation was observed in females of all handled groups. Handling plus exposure to elevated ambient temperature (30 deg C or 31 deg C) during days 6-15 of gestation increased this reduction in maternal weight gain.

A significant decrease in implantation sites per litter and reduction in fetal weight was noted in the group exposed to 30 mW/sq cm during days 1-6 of gestation. Exposure of mice to a power density of 30 mW/sq cm (days 6-15 of gestation) resulted in a slight, but significant increase in the percentage of malformed fetuses, predominantly with cleft palate, when compared to all other groups.

**

Study Type: Teratology and Developmental Abnormalities;
IN VIVO; MOUSE
Effect Type: RFR- and temperature-induced effects on maternal weight gain; litter size; numbers of implantation sites, resorptions, and live and dead fetuses; and induced fetal anomalies
Frequency: 2.45 GHz
Modulation: CW
Power Density: 5, 21, or 30 mW/sq cm
SAR: 6.7, 28.14, or 40.2 W/kg

EXPOSURE CONDITIONS: Groups of pregnant mice in individual Styrofoam cages were exposed in circular arrays to far-field RFR in an anechoic chamber for 8 hr/day at 5 mW/sq cm during gestational days 1-15, or at 21 or 30 mW/sq cm during gestational days 1-6 or 6-15, all at 22 deg C ambient temperature and 55% relative humidity. Other groups were sham-exposed under the same conditions. Still others were exposed to 30 or 31 deg C ambient temperature without RFR.

OTHER INFORMATION: The power density at each location in the array was measured with an NBS probe with the mouse absent but with the mice present in the other locations. The mice were spaced at least 2 wavelengths apart, and no power density changes were detected at each location due to the presence or movement of the mice in the other locations. Spatial variations of power density over the circular array were about 10%. The SARs cited above were for mice curled up (asleep), the configuration taken during most of each exposure period.

Groups for each treatment were characterized as "handled" or "nonhandled". Handled mice were transferred to Styrofoam cages (one per cage) for RFR-, sham-, or heat-exposure during 0800-1200 and 1300-1700, and were housed in polycarbonate shoe-box-type cages for feeding and watering during 1200-1300 and for the remainder of each 24-hr period. Nonhandled mice were housed in the latter type of cage for the entire period. Body weights were recorded on gestational days 1, 6, 15, and 18. On day 18, the dams were euthanized and the implantation sites, resorptions, dead, and live fetuses were counted. The fetuses were sexed, weighed, and examined for malformations.

In the first experiment, mice were exposed at 5mW/sq cm for 8 hr/day during gestational days 1-15 (RFR-exposed-handled-group). Two groups designated as sham-exposed-handled and sham-exposed-nonhandled served as controls. The pregnancy rates, maternal weight gains, and average fetal weights for both handled groups were lower than for the nonhandled group. No significant differences were found among the 3 groups in the other parameters.

In the second experiment, handled groups were exposed to RFR at 21 mW/sq cm or to an ambient temperature of 30 deg C (the latter selected to yield the same rectal temperature increase, about 1 deg C, as the former) and a nonhandled group was exposed at 30 deg C, all three during gestational days 1-6. Three other groups were similarly treated during gestational days 6-15. Again, sham-exposed-handled and sham-exposed-nonhandled groups served as controls. For those treated on days 1-6, significantly smaller maternal weight gains were seen in the 3 handled groups (RFR-exposed, sham-exposed, temperature-exposed) relative to the 2 nonhandled groups (sham-exposed, temperature-exposed). For those exposed on days 6-15, the maternal weight gain was smaller for the temperature-exposed-nonhandled group as well, and the greatest decrease was for the temperature-exposed-handled group. The other parameters were not affected significantly.

The third experiment was similar to the second, but with 30 mW/sq cm and 31 deg C (yielding a rectal temperature increase of 2.3 deg C). For mice treated on days 1-6, the handled groups gained significantly less weight than the nonhandled groups; the RFR-exposed (handled) group had significantly fewer implantation sites per litter than the sham-exposed-nonhandled group; and the reduction in fetal weight for the RFR-exposed group was comparable to that for the temperature-exposed-handled group. No increases in external, visceral, or skeletal malformations were seen in any group. The results for mice treated on days 6-15 were similar except that the average percentage of malformed fetuses for the RFR-exposed group was significantly larger than for any other group, with cleft palate the predominant malformation.

The investigators concluded that for RFR exposure during gestational days 6-15, the threshold for induction of teratogenic effects in CD-1 mice is about 30 mW/sq cm (SAR about 40 W/kg).

CRITIQUE: In the first two experiments (5 or 21 mW/sq cm, or 38 deg C), handling the mice (as described) appears to have been the primary factor that contributed to the differences in mean fetal weights, but the results were not entirely consistent. For example, in the first experiment (Table 2), the mean fetal weight for the sham-exposed-nonhandled group was significantly higher than for either the sham-exposed-handled or the RFR-exposed (5 mW/sq cm) group. However, for the group exposed on days 6-15 in the second experiment (Table 5), the values for the sham-exposed-nonhandled and the sham-exposed-handled groups were lower than for the RFR-exposed (21 mW/sq cm) group. In addition, there was no significant difference between the nonhandled and handled groups treated at 30 deg C.

The results of treatment during days 1-6 in the third experiment (Table 7) indicated that both handling and treatment with RFR (30 mW/sq cm) or elevated temperature (31 deg C) decreased mean fetal weight. In addition, the number of implantation sites per litter in the RFR-exposed group was significantly lower than for the sham-exposed-nonhandled group but not for the sham-exposed-handled group. By contrast, similar treatments during days 6-15 (Table 8) yielded no significant differences in either endpoint among any of the groups.

Thus, it is difficult to compare these results on mean fetal weight with those of Berman et al. (1978, 1982), who used the same mouse strain and found about 10% reduction in this endpoint from exposure at 28 mW/sq cm during days 6-17. Also, Nawrot et al. (1981) did not allow any of the dams to come to term, so the stunting of neonates reported by Berman et al. was not investigated.

Probably the most important finding of Nawrot et al. was the significantly larger percentage of malformed fetuses for the group exposed at 30 mW/sq cm during days 6-15. Qualitatively similar results (but cranioschisis rather than cleft palate as the most frequent malformation) were reported by Berman et al. in 1978, but none in 1982.

It should be noted that in the exposure system used by Berman et al., the spatial variations of power density and SAR were much larger than in the system used by Nawrot et al., so the estimated threshold for such teratogenic effects by the latter is probably more accurate than estimates from the data of the former.

REFERENCES:
Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982)

Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978)

***

NAWROT
MCREE
STAPLES

/

CW
DEVELOPMENT
EMBRYO
HYPERTHERMIA
IN-VIVO
MOUSE
RFR
TERATOGENIC
WEIGHT

//

1981
2450
1
5-30
6.7-40.2

///

87
Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980)

*

AUTHOR ABSTRACT: Although exposure to nonionizing electromagnetic radiation has been reported to cause a variety of systemic alterations during embryonic development, there are few reports of the induction of specific physiologic or morphologic changes in the myocardium. This study was designed to examine the effects of microwave radiation on cardiogenesis in Japanese quail embryos exposed during the first eight days of development to 2.45-GHz continuous-wave microwaves at power densities of 5 or 20 mW/sq cm. The specific absorption rates were 4.0 and 16.2 mW/g, respectively. The ambient temperature for each exposure was set to maintain the embryonated eggs at 37.5 deg C. This did not preclude thermal gradients in the irradiated embryos since microwaves may not be uniformly absorbed.

The test exposure levels did not induce changes in either the morphology of the embryonic heart or the ultrastructure of the myocardial cells. Analysis of the enzymatic activities of lactate dehydrogenase, glutamic oxaloacetic transaminase, and creatine phosphokinase failed to reveal any statistically significant differences between the nonexposed controls and those groups exposed to either 5 or 20 mW/sq cm. The data indicate that 2.45-GHz microwave radiation at 5 or 20 mW/sq cm has no effect on the measured variables of the Japanese quail myocardium exposed during the first eight days of development.

**

Study Type: Teratology and Developmental Abnormalities, Cardiovascular Effects, Physiology and Biochemistry; IN VIVO; JAPANESE QUAIL
Effect Type: RFR-induced changes in the morphology of the embryonic heart, the ultrastructure of the myocardial cells, or enzymatic activities
Frequency: 2.45 GHz
Modulation: CW
Power Density: 5 or 20 mW/sq cm
SAR: 4.03 or 16.12 W/kg

EXPOSURE CONDITIONS: 6 X 5 arrays of eggs were exposed in the far field at 60% relative humidity and ambient temperature selected to maintain the eggs at 37.5 deg C (optimum for development). Each array was exposed 24 hr/day for 8 days, and was turned 90 deg every 2 hr. Three arrays were exposed at each power density. Control arrays were sham-exposed concurrently with the RFR-exposed arrays, but otherwise treated similarly.

OTHER INFORMATION: The 8-day exposure duration was chosen to encompass the organogenesis period, during which the embryo is most sensitive to teratogenic agents. As in previous studies by this group (e.g., McRee and Hamrick, 1977), each array was exposed with the major axes of the eggs parallel to the electric field, and the arrays were turned 90 deg about the propagation direction every 2 hr, which placed the major axes parallel to the magnetic field for half the entire exposure duration.

Following exposure, the embryos were removed, weighed and examined. No significant differences in mean weight among the RFR- and sham-exposed groups and no gross morphologic abnormalities were found. The hearts were removed, homogenized, and assayed for protein content and activities of the enzymes lactate dehydrogenase, glutamic oxaloacetic transaminase, and creatine phosphokinase. No statistically significant differences in these activities (expressed per unit of protein content) were found among the groups exposed at 20, 5, or 0 (sham) mW/sq cm. The right atrium and right ventricle of several RFR- and sham-exposed specimens were excised, fixed, sectioned, and examined with an electron microscope. The specimens exposed at either power density had myocardial cytoarchitectures comparable to those of the sham-exposed specimens. This was also true for atrial and ventricular tissues.

CRITIQUE: These negative findings support the results of McRee and Hamrick (1977), but appear to be at variance with the findings of Carpenter and Livstone (1971), Liu et al. (1975), and Fisher et al. (1979). The key issue addressed by Galvin et al. in this investigation is careful maintenance of embryonic temperature at its optimum value (37.5 deg C) during RFR (or sham) exposure. When this was done, no teratogenic effects or developmental abnormalities were observed down to the ultrastructural level. By inference, the positive findings of others can be ascribed to RFR-induced excessive embryonic temperatures or to lack of adequate temporal or spatial control over embryonic temperatures during exposure.

REFERENCES:

Carpenter, R.L. and E.M. Livstone
EVIDENCE FOR NONTHERMAL EFFECTS OF MICROWAVE RADIATION: ABNORMAL DEVELOPMENT OF IRRADIATED INSECT PUPAE
IEEE Trans. Microwave Theory and Tech., Vol. 19, No. 2, pp. 173-178 (1971)

Fisher, P., J.K. Lauber, and W.A.G. Voss
THE EFFECT OF LOW-LEVEL 2450 MHZ CW MICROWAVE IRRADIATION AND BODY TEMPERATURE ON EARLY EMBRYONAL DEVELOPMENT IN CHICKENS
Radio Sci., Vol. 14, No. 6S, pp. 159-163 (1979)

Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE RELATION OF TERATOGENESIS IN TENEBRIO MOLITOR TO THE INCIDENCE OF LOW-LEVEL MICROWAVES
IEEE Trans. Microwave Theory and Tech., Vol. 23, No. 11, pp. 929-931 (1975)

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)

***

GALVIN
MCREE
LIEBERMAN

/

BIOCHEMISTRY
CARDIAC
CW
DEVELOPMENT
EMBRYO
IN-VIVO
PHYSIOLOGY
QUAIL
RFR
TERATOGENIC

//

1980
2450
1
5-20
4.03-16.1

///

88
Fisher, P., J.K. Lauber, and W.A.G. Voss
THE EFFECT OF LOW-LEVEL 2450 MHZ CW MICROWAVE IRRADIATION AND BODY TEMPERATURE ON EARLY EMBRYONAL DEVELOPMENT IN CHICKENS
Radio Sci., Vol. 14, No. 6S, pp. 159-163 (1979)

*

AUTHOR ABSTRACT: The effects of 2450-MHz irradiation (3.5 mW/sq cm) on cranial length and wet mass of four- and five-day embryos at different incubation temperatures (32 to 36 deg C) were investigated. A temperature-dependent effect on growth rate was observed. At 36 deg C, final cranial lengths and wet mass of experimental embryos were found to be below those of controls after four and after five days of incubation; however, the rate of growth was higher than that of controls. At 32 deg C, the final values of cranial length and wet masses were higher than the control values after four and after five days of incubation while the rate of growth was lower. It is concluded, after comparing wet-mass data with cranial-length data, that the developmental rate of the whole embryo was affected, and that the effect was a result of some mechanism not associated with an incremented temperature of the embryo.

**

Study Type: Teratology and Developmental Abnormalities;
IN VIVO; CHICKEN
Effect Type: RFR-induced changes in cranial length and wet mass of embryos
Frequency: 2.45 GHz
Modulation: CW
Power Density: Spatial average 3.46 mW/sq cm (range 1.4-6.2 mW/sq cm)
SAR: Not measured

EXPOSURE CONDITIONS: 6 X 6 arrays were exposed for 24 hr/day for 4 or 5 days to the far field of a horn in an anechoic chamber. The arrays were in a specially designed Plexiglas-and-Styrofoam incubator with its temperature and relative humidity maintained by circulating air through flexible plastic hoses. The relative humidity in the incubator was 73%. Incubator temperatures at egg sites ranged from 32 to 36 deg C but was constant at each site. The long axis of each egg was in a plane parallel to both the propagation and electric vectors and tilted 30 deg relative to the electric vector. All axes were shifted to the symmetric 30-deg orientation every 24 hr.

OTHER INFORMATION: The optimal incubation temperature for chicken embryos is about 38 deg C. Suboptimal incubator temperatures were used to compensate for additional heat from RFR absorption and thereby minimize the possible occurrence of abnormalities from excessive temperatures. Embryo temperature was measured by inserting a thermocouple through an opening in the shell. This was done for 6 sample eggs in the 6 X 6 array at the end of the 4- or 5-day incubation

period, within 30 seconds after opening the incubator. The spatial temperature variation within the incubator was used to estimate the temperatures of the other 30 embryos. Sham-exposed arrays served as controls.

The embryos were then excised, the extraembryonic membranes were removed, the wet mass of each embryo was measured, and the embryo was photographed. Cranial lengths were measured on tenfold enlargements. Empirical formulas relating each endpoint (wet mass and cranial length) separately to the Hamilton-Hamburger stage (HHS) of development were used to determine the HHS values. Type II regression analysis for ungrouped data (Sokal and Rohlf, 1969) was used because the embryo temperature (controlled variable) was subject to error, and the regression lines for HHS versus embryo temperature were compared.

For the eggs incubated for 4 days at an embryo temperature of 32 deg C, the stage of development (HHS value) of the RFR-exposed eggs was significantly later than for the unexposed controls. The converse was true at 36 deg C, with the regression lines crossing (same HHS value) at about 34 deg C. Similar results, but at larger HHS values, were obtained for the eggs incubated for 5 days. These results appeared to indicate that the RFR had advanced the stage of development at 32 deg C, did not affect it at 34 deg C, and retarded it at 36 deg C. The authors also stated that the frequency of premature deaths and of sterility did not differ significantly among groups.

CRITIQUE: It is difficult to analyze these results because the investigators had not included their temperature measurements of the 6 sample embryos, the locations of these eggs in the array, and the calculated temperatures of the other embryos. For the range of power densities in the array (1.4 to 6.2 mW/sq cm) it seems likely that the distribution of embryo temperatures over an RFR-exposed array should be significantly different from the distribution for an unexposed array, and the differences might serve as coarse measures of SARs.

It is also difficult to assess the range of applicability of the empirical equations for HHS because they were taken from an unpublished reference (Demorest, 1977). In the absence of such information, the results of these investigators could be accepted at face value, except that they differ from those of other investigators, such as McRee and Hamrick (1977), and Galvin et al. (1980), who found no teratogenic or developmental effects from RFR exposure of Japanese quail eggs to higher power densities at the same frequency when the embryo temperatures were maintained constant at the optimal incubation value during RFR (and sham) exposure.

REFERENCES:
Demorest, D.L.
A FLUOROMETRIC INVESTIGATION OF EARLY CHICKEN EMBRYO DEVELOPMENT
Unpublished (1977)

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)

Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980)

***

FISHER
LAUBER
VOSS

/

CHICKEN
CW
DEVELOPMENT
EMBRYO
IN-VIVO
RFR
TERATOGENIC
WEIGHT

//

1979
2450
1
1.4-6.2
0

///

89
Lester, J.R. and D.F. Moore
CANCER MORTALITY AND AIR FORCE BASES
J. Bioelectricity, Vol. 1, No. 1, pp. 77-82 (1982a)

*

AUTHOR ABSTRACT: Nationally, counties with an Air Force base were found to have significantly higher incidences of cancer mortality during 1950-1969 compared with counties without an Air Force base.

**

Study Type: Human Studies; Mutagenesis, Carcinogenesis, and Cytogenetic Effects; Environmental Factors; IN VIVO; HUMAN
Effect Type: Examination of cancer mortality statistics for U.S. counties for the period 1950-1969 to see whether there was an increase in cancer mortality in counties with an Air Force base when compared with population-size-matched counties from the same state not having an Air Force base
Frequency: Not specified, other than "Air Force base radar transmissions"
Modulation: Pulsed (implied from "radar transmissions")
Power Density: Not stated
SAR: Not stated

EXPOSURE CONDITIONS: Chronic exposure of populations in county in which an Air Force base is located

OTHER INFORMATION: Lester and Moore postulated that prolonged, repeated exposure to weak RFR might be associated with increased cancer incidence. Because radar has been in operation at military air bases since World War II, one might therefore expect to find a detectable increase in cancer mortality in areas surrounding air bases. To test this hypothesis, the authors selected Air Force Bases (AFBs) in the continental United States operational in the period 1950-1969 and found 92 counties containing at least one AFB. The population of each of these counties was determined using the 1960 census. A control county was determined as one from the same state nearest in population(sometimes larger, sometimes smaller) to the AFB county, but not containing an AFB. Other military or civilian air bases may have been present in either AFB or control counties, but these would have biased the results against the hypothesis.

Cancer mortality ratings (deaths from all types of cancer) for AFB and control counties were obtained from the "Atlas of Cancer Mortality for U.S. Counties: 1950-1969" (U.S. Dept. of Health, Education, and Welfare, 1975). These mortality data were age adjusted and presented in the following five categories with respect to cancer mortality in the general U.S. population:

MORTALITY RANKING	LESTER AND MOORE INDEX
Significantly high, in highest decile	4
Significantly high, not in highest decile	3
In highest decile, not significant	2
Not significantly different from U.S.	1
Significantly lower than U.S.	0

Data were available separately for males (M) and females (F). Lester and Moore presented the following results (their Table 1):

TABLE 1

	MALES		FEMALES		INDEX
	Counties		Counties		
	AFB	nonAFB	AFB	nonAFB	
	21	12	13	7	4
	2	1	4	2	3
	5	6	0	3	2
	16	21	33	34	1
	48	52	42	46	0
Totals	92	92	92	92	

From examination of these results, Lester and Moore made the following assumptions:

"a. Categories 4 and 3 can be combined as significant incidence (+); categories 1 and 0 as nonsignificant incidence (-).

b. Category 2 can be deleted.

c. Since there was an effort to match counties by population, the proper statistical analysis is a test for correlated proportions comparing AFB with nonAFB counties."

Reclassifying their data in pairs, Lester and Moore presented their Table 2:

TABLE 2

INCIDENCE	M	F
AFB (+) and nonAFB (+)	9	7
AFB (-) and nonAFB (-)	57	70
AFB (+) and nonAFB (-)	12	10
AFB (-) and nonAFB (+)	4	2
Totals	82	89

Their analysis of the data in their Table 2 ("test for correlated proportions, corrected for continuity, one-tailed test") yielded p=0.04 for males, p=0.02 for females. Hence, Lester and Moore concluded that counties with an AFB, when compared with population-matched counties without an AFB, have significantly higher incidence of cancer mortality for the period 1950-1969.

CRITIQUE: This paper is one of only a few in the scientific literature to suggest that RFR exposure is linked with increased cancer incidence and mortality. However, as presented, the results do not confirm that increased cancer mortality is associated with RFR exposure, but only that such mortality appears to be correlated with the presence of an operational AFB.

The test for a statistically significant difference between AFB and control counties depends heavily on how well the control counties were matched with the AFB counties in all factors except presence of an AFB. The identities of the AFBs were not given in the paper, so we corresponded with Dr. J. Lester, who kindly made available his raw data. In reviewing these data, it became apparent there were several inconsistencies, so we conducted our own analysis using the same list of AFBs provided by Dr. Lester and the same methodology described in his paper.

We ascertained the counties in which the AFBs were located by using a Rand McNally Commercial Atlas. Populations of these counties were determined from the same reference as Lester and Moore (County and City Data Book, 1967), and control counties nearest in population in the same state were identified. Cancer mortality categories for control and AFB counties, for males and females, were obtained from the same reference as Lester and Moore (Atlas of Cancer Mortality for U.S. Counties: 1950-1969).

At the conclusion of this reassembly of the raw data, the following emerged:

1. The total number of AFB counties is reduced to 91 because one county was counted twice (Luke AFB and Williams AFB are in the same county).

2. Of these 91, 13 AFBs were located by Lester and Moore in incorrect counties.

3. Of the remaining 78, in 43 cases either the incorrect control county was used (supposed to be nearest in population, larger or smaller, in same state, not having an AFB), or the M or F category assigned to the control county by Lester and Moore was incorrect.

4. Of the remaining 35 cases where we agreed with the Lester and Moore selection of AFB and control counties, there were 22 cases (16 counties) where we disagreed with the M or F categories assigned by Lester and Moore.

Thus, of the original 92 AFB/control county pairs of data used by Lester and Moore, we agreed with only 19 of these pairs and their M and F categories.

Using the corrected data for the 91 AFB counties, we obtained the following revised Table 1:

REVISED TABLE 1

	MALES		FEMALES		INDEX
	Counties		Counties		
	AFB	nonAFB	AFB	nonAFB	
	16	10	9	7	4
	0	1	3	3	3
	6	8	0	2	2
	17	24	33	36	1
	52	48	46	43	0
Totals	91	91	91	91	

With the same assumptions used by Lester and Moore (see OTHER INFORMATION section) we reclassified these data and obtained:

REVISED TABLE 2

INCIDENCE	M	F
AFB (+) and nonAFB (+)	6	6
AFB (-) and nonAFB (-)	58	73
AFB (+) and nonAFB (-)	10	6
AFB (-) and nonAFB (+)	6	5
Totals	80	90

We consulted with a statistician about the "test for correlated proportions" used by Lester and Moore. Such a test does not appear by this name in any of the references we or he are familiar with. However, McNemar's Test (Fleiss, 1981) is suitable and is similar to the test by Lester and Moore because use of this test yielded the same z and p values cited by Lester and Moore for their Table 2. Use of McNemar's Test for the data of revised Table 2 yielded: for males, $z=0.7$, $p=0.23$; for females, $z=0$, $p=0.50$.

Thus, a complete reanalysis of data for 91 AFB counties used by Lester and Moore and the population-matched control counties not having an AFB did not confirm Lester and Moore's finding. Instead, counties with an AFB had incidences of cancer mortality that were not statistically significantly different from incidences of cancer in population-matched counties without an AFB for the period, 1950-1969, for either males or females. The original finding of significance by Lester and Moore was apparently the result of an incorrectly assembled data base.

REFERENCES:
Air Force Magazine
GUIDE TO AIR FORCE BASES
Air Force/Space Digest, pp. 221-239 (September 1969)

Fleiss, J.L.
STATISTICAL METHODS FOR RATES AND PROPORTIONS
2nd Edition, John Wiley and Sons, New York (1981)

Rand McNally and Company
1982 COMMERCIAL ATLAS AND MARKETING GUIDE
113th Edition (No. 113 07949), Chicago, New York, San
Francisco (1982)

U.S. Bureau of the Census
COUNTY AND CITY DATA BOOK,1967 (A STATISTICAL ABSTRACT SUPPLEMENT),
U.S. Government Printing Office, Washington, D.C. (1967)

U.S. Department of Health, Education, and Welfare
ATLAS OF CANCER MORTALITY FOR U.S. COUNTIES: 1950-1969 DHEW Publication
No. (NIH) 75-780, National Cancer Institute, Washington, D.C. (1975)

***

LESTER
MOORE

/

CARCINOGENIC
CYTOGENETIC
EPIDEMIOLOGIC
HUMAN
IN-VIVO
MODULATED
MORBIDITY
MORTALITY
MUTAGENIC
PULSED
RFR

//

1982
0
0
0
0

///

90
Bielski, J., A. Sawinska, and J. Pianowska
BIOELECTRICAL BRAIN ACTIVITY IN EMPLOYEES EXPOSED TO VARIOUS FREQUENCIES OF ELECTROMAGNETIC FIELDS
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 193-195 (June-July 1980)

*

AUTHOR ABSTRACT: In 28% employees, exposed to microwaves 3 000 - 7 000 MHz and 0.1 - 2 W/sq m power density, in the EEG record of the deep leads, single short series of slow theta waves were found. In 69% industry employees, exposed to electromagnetic fields of 7 - 30 MHz frequency and 30 - 200 V/m intensity, in the high voltage EEG record of the deep leads, numerous series of slow theta waves and single sharp waves /"spikes"/ were found. This may indicate a more harmful influence upon brain activity of longer waves as compared to microwaves.

**

Study Type: Human Studies, Ocular Effects, Nervous System; IN VIVO; HUMAN
Effect Type: Alteration of EEG records of persons occupationally exposed to RFR when compared with nonexposed control groups. Increased complaints of different nonspecific symptoms--excessive irritability, increased perspiration, headaches, dizziness, etc.--called "symptoms of vegetative neurosis" in exposed versus control groups
Frequency: (1) 3 to 7 GHz; (2) 7 to 30 MHz
Modulation: (1) Specified only as "radio and television installations"; (2) Specified only as "wood glueing elements in furniture industry"
Power Density: (1) 0.01 to 0.2 mW/sq cm; (2) 30-200 V/m (equivalent to 2.3-10 mW/sq cm)
SAR: Not specified

EXPOSURE CONDITIONS: (1) Occupational exposure from 1 to 20 years of 88 employees operating radio and television installations with the microwave frequency range of 3 to 7 GHz. Average exposure time was about 170 hr per month. (2) Occupational exposure from 1 to 16 years of 68 furniture industry workers working with wood glueing equipment. Average exposure time was about 100 hr per month.

OTHER INFORMATION: The authors undertook a study of the effects of chronic occupational exposure to RFR with particular emphasis on effects on the EEG. Two groups of workers were studied. The first (88 persons) had been exposed from 1 to 20 years to microwaves in the range from 3 to 7 GHz at 0.01 to 0.2 mW/sq cm for about 170 hr per month. The second (68 persons) had been exposed from 1 to 16 years to HF RFR in the range from 7 to 30 MHz at 30-200 V/m (approximately 0.2 to 10 mW/sq cm) for about 100 hr per month. Thirty-nine persons of similar age and work experience, but without RFR exposure, served as controls for the microwave group. Forty-one similarly matched unexposed persons served

as controls for the HF group. All persons underwent a general medical, ophthalmological, neurological, and psychological examination.

The results showed that most of the employees exposed to microwaves and HF RFR complained of non-specific symptoms--headaches, excessive irritability, increased perspiration, discomfort and sleep disturbances. The RFR subjects also complained of dizziness, heartache, lack of concentration, etc., the total symptoms being called "typical symptoms of vegetative neurosis" by the authors. Non-normal EEGs (series of slow theta waves) were found in 28% of the microwave subjects versus 20% of the control subjects. Likewise, non-normal EEGs (slow theta waves and "spikes") were observed in 69% of the HF-exposed subjects versus none of the HF-control subjects. The authors stated that the frequency of anomalous EEG records and the intensity of EEG changes were markedly higher among the HF-exposed workers than among the microwave-exposed workers, and that this may indicate a more harmful influence upon brain activity of HF RFR as compared with microwaves.

CRITIQUE: There are several major obstacles in assessing this study. Persons employed in the radio and television broadcast industry are generally not exposed to microwaves in the 3-7 GHz bands, but rather may be exposed to the AM, FM, and TV bands (all below 1 GHz). Microwave frequencies may be encountered in low-power (approx. 10 W total power) relay links from studios to broadcast tower sites, or from mobile units to studios. However, these links are highly directional. The exposure levels cited for microwave-exposed subjects are unlikely to be attributable to microwaves. More likely is that they are associated with the broadcast frequencies mentioned above.

Another problem is that no statistical tests on the data are reported. Whether the differences between exposed and controls are statistically significant is not indicated. Further, whether the differences may be related to other factors is unclear. For example, the subjects from the furniture industry who were involved with the operation of wood glueing equipment were also likely exposed to fumes and vapors from the solvents in the glues. That the control group for the furniture industry, selected for similar work experience, showed no changes in EEG or other parameters is therefore surprising in view of their potential exposure to thinners, lacquers, varnishes, etc. Adequacy of controls may also be questioned in view of the fact that there is wide divergence between the two control groups in so-called non-normality (20% of the microwave control group versus 0% of the HF control group).

Although it was stated that all persons were given ophthalmological tests, no mention was made of the results of these tests, leading to the assumption that there were no differences between exposed and control subjects. Finally, it can be noted that all of the furniture industry workers using wood glueing equipment were exposed for many years at levels considerably above the Polish standards (Stuchly and Repacholi, 1978) and that these HF exposure levels were two orders of magnitude above the microwave exposure levels.

In summary, the suggestion that there are effects on the EEG from chronic exposure to RFR is not substantiated by this paper. The authors themselves recommended that "larger groups and analysis according to age, time of exposure and social standards are needed to answer whether this (effect) is directly related to occupational exposure to radiofrequency radiation."

REFERENCE:
Stuchly, M.A. and M.H. Repacholi
MICROWAVE AND RADIOFREQUENCY PROTECTION STANDARDS
In MICROWAVE BIOEFFECTS AND RADIATION SAFETY,
Trans. IMPI, Vol. 8, pp. 95-101 (1978)

***

BIELSKI
SAWINSKA
PIANOWSKA

/

CHRONIC
EEG
EPIDEMIOLOGIC
HUMAN
IN-VIVO
MODULATED
NERVOUS-SYSTEM
OCULAR
OCCUPATIONAL
PHYSIOLOGY
RFR

//

1980
7-7000
0-1
0.01-10
0

///

91
Lester, J.R. and D.F. Moore
CANCER INCIDENCE AND ELECTROMAGNETIC RADIATION
J. Bioelectricity, Vol. 1, No. 1, pp. 59-76 (1982b)

*

AUTHOR ABSTRACT: A neighborhood pattern of cancer incidence was found in the city of Wichita, Kansas with the suggestion of a time element in its appearance. Cancer tended to occur on leading terrain crests relative to radar transmissions and was less frequent in the valleys. A formula is presented that relates the incidence of cancer, terrain, and the presence of microwave radiation.

**

Study Type: Human Studies; Mutagenesis, Carcinogenesis, and Cytogenetic Effects ; IN VIVO; HUMAN
Effect Type: Correlation between cancer incidence and airport radar exposure in the population of Wichita, Kansas
Frequency: Not given
Modulation: Not given
Power Density: Not measured
SAR: Unknown

EXPOSURE CONDITIONS: Assumed to be chronic exposure of the general population to airport radar emissions

OTHER INFORMATION: This study was undertaken in an attempt to find a possible connection between cancer incidence and external electromagnetic fields. The approach involved examining whether there was a geographic pattern of cancer incidence within Wichita, Kansas, and whether specific sources of electromagnetic radiation could be identified and related to any cancer incidence patterns. The authors are associated with the University of Kansas School of Medicine in Wichita.

Wichita is the largest city in Kansas (population 262,766--from a 1973 census). With the exception of two industrial areas, it is divided into 94 census tracts of approximately equal population. (Only 76 tracts were included in the present analysis, though.) The tracts have been stratified into three health and economic classes (good, fair, poor) by the Department of Community Health based on determinants such as education, income, crowding, unskilled workers, infant mortality, venereal disease, tuberculosis, and housing. Wichita is virtually free of air pollution (ranked second out of 52 major cities of over 80,000 population in the U.S.A.), presumably removing air pollution as a confounding factor in this study.

The city lies on essentially a flat plain bisected by the Arkansas River, with two low ridges (100-ft and 20-ft elevation changes) to the west and northwest of the city limits. Wichita Mid-Continent Airport

lies 9.7 km southwest and 35 ft higher than Wichita's city center. McConnell Air Force Base (AFB) lies 7.2 km southeast and 130 ft higher than the city center.

Morbidity data were obtained on all first diagnosed cancer cases of Wichita residents for 1975, 1976, and 1977 from 5 city hospitals, a total of 3004 cases for the 3 years. The ratio of number of diagnosed cases to tract population for each year yielded incidence rates for 76 census tracts. Information on incidence rates, age, economic stratification (of the tract of residence of the individual), male/female ratio, and race were analyzed and a correlation matrix obtained for the 76 tracts.

Mortality data were obtained for all cancer deaths of Wichita residents for 1975, 1976, and 1977. Again incidence rates, age, economic stratification, male/female ratio, and race were analyzed, and a correlation matrix obtained for the 76 census tracts.

The authors' treatment of data purporting to relate cancer to exposure to electromagnetic radiation is rather involved. The authors proposed several hypotheses. First, the major contributors to electromagnetic radiation exposure are radar transmitters at the airports. Second, radar exposure is a line-of-sight phenomenon. Third, exposure correlates directly with elevation. Fourth, shielding by intervening terrain confounds the simple exposure criterion of elevation. Their "Shield" and "Criterion Measures" for RFR exposure levels and the validity of their hypotheses are discussed in the critique.

CRITIQUE: The overall finding of this paper is that for the population of Wichita, Kansas, cancer incidence appears related to the probability of exposure to radar. However, this paper is replete with flaws that vitiate such a finding.

The most serious flaw is that, in attempting "to find a possible connection between cancer incidence and external electromagnetic fields," the authors assumed that the population is exposed only to electromagnetic radiation from radars at the two airports adjacent to the city. No actual measurements had been made to support this assumption. Measurements of ambient levels of RFR were made by the Environmental Protection Agency (EPA) in 15 major cities around the U.S.A. (Tell and Mantiply, 1980). These measurements showed that by far the major contributors to environmental levels of RFR are FM and TV broadcast transmitters, not radar systems (Janes, 1979). Although EPA did not include Wichita, Kansas, as one of the cities it surveyed, it is reasonable to assume that the RFR environmental situation there differs little from the other 15 cities surveyed.

The hypothesis that the authors have chosen (by virtue of ignoring sources other than the radars) is that cancer incidence is related to exposure to RFR only from the airport radars. To test this hypothesis, one should use a model of RFR exposure that uses the physical laws

associated with RFR propagation; most importantly, inverse-square-law attenuation with distance, the shielding effects of manmade structures and buildings as well as of terrain, and knowledge of the scan sectors of radars. Unfortunately, the model used by the authors bears no relationship to these factors, and any conclusions to be drawn from its use are unrelated to actual exposure levels. The results from this paper may therefore be considered a good example of spurious correlation. Other flaws in the paper are in the arbitrary assumptions made for the heights of the radars, and the false sense of precision given by citing elevations of the city and airports to 5 significant figures ("average" elevations accurate to within 5 mm). The relationship claimed by the authors between radar exposure and cancer incidence may exist. However, it is not demonstrated by the data and analysis presented in this paper.

REFERENCES:

Tell, R.A. and E.D. Mantiply
POPULATION EXPOSURE TO VHF AND UHF BROADCAST RADIATION IN THE UNITED STATES
Proc. IEEE, Vol. 68, No. 1, p. 6 (1980)

Janes, D.E., Jr.
RADIATION SURVEYS--MEASUREMENTS OF LEAKAGE EMISSIONS AND POTENTIAL EXPOSURE FIELDS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, p. 1021 (1979)

***

LESTER
MOORE

/

CARCINOGENIC
CHRONIC
CYTOGENETIC
EPIDEMIOLOGIC
HUMAN
IN-VIVO
MODULATED
MORBIDITY
MORTALITY
MUTAGENIC
PULSED
RFR

//

1982
0
0
0
0

///

92
Milham, S., Jr.
MORTALITY FROM LEUKEMIA IN WORKERS EXPOSED TO ELECTRICAL AND MAGNETIC FIELDS (Correspondence)
New England J. Med., Vol. 304, p. 249 (1982)

*

REVIEWER SUMMARY: All deaths of Washington State resident white males age 20 years or older in the period from 1950 through 1979 were coded according to occupation. Mortality ratios (observed/expected) standardized by age and by year of death were calculated for 158 cause-of-death groups in each of 218 occupational classes. In all, 438,000 deaths were analyzed. Examination of mortality from acute leukemia and from all leukemia for 11 occupations with presumed exposure to electrical or magnetic fields showed an elevation in 18 of the 22 categories. The author of this letter was unaware of any obvious leukemogenic exposures in these occupations, and believed that the data suggest that electrical and magnetic fields may cause leukemia.

**

Study Type: Human Studies; Mutagenesis, Carcinogenesis, and Cytogenetic Effects ; IN VIVO; HUMAN
Effect Type: Increased incidence of mortality from all leukemia for 11 occupations with presumed exposure to electric or magnetic fields
Frequency: Unknown (implied as being DC through UHF)
Modulation: Unknown
Power Density: Unknown
SAR: Unknown

EXPOSURE CONDITIONS: Occupational

CRITIQUE: The scientific literature contains very few claims that exposure to electric and magnetic fields causes cancer. This report, in the form of a Letter to the Editor of the New England Journal of Medicine, is therefore of significant interest. Similar epidemiologic techniques have been used with success to relate cancer incidence with exposure to certain agents, e.g.,cancer of the liver with vinyl chloride exposure, mesothelioma with asbestos exposure, etc. The letter provides very little detail on specifics of the treatment of the data. The author has apparently used well established techniques to standardize mortality by age and year of death against "standard" population (Lilienfeld and Lilienfeld, 1980). Data are presented on 136 observed leukemia deaths out of a total of 438,000 deaths from all causes for Washington State adult white males from 1950 through 1979. Using the given values for observed and expected mortality, it is possible to calculate the statistical significance of the proportionate mortality ratio from formulas in Lilienfeld and Lilienfeld (1980). These calculations confirm, in general, the significance levels tabulated by the author.

Given that there is, indeed, an excess of deaths from acute leukemia and from all leukemia in the 11 occupations reported, it is necessary to examine whether the excess deaths are related to exposure to electric and magnetic fields as claimed. For a cause and effect relationship to be established, epidemiologic methodology requires that a quantitative relationship exist, i.e., increased incidence of leukemia with increased exposure to electric and magnetic fields. Such a relationship is at best unproven in the data presented. It is the assumption of this report that persons having these occupational categories on their death certificates were exposed more to electric and magnetic fields than were individuals in other occupational categories. Such assumptions may not necessarily be correct. For example, the largest group in the report (51 observed deaths) is "Electricians." However, electricians perform most of their work on circuits that are not energized, i.e., in the (relative) absence of electric and magnetic fields. And contrary to the stated hypothesis, arc welders (who do spend considerable time in close proximity to magnetic fields from the large currents their welders generate) show a considerable reduction in proportionate mortality data. In the absence of more specific information on exposures of the individuals in these categories (frequencies, intensities, electric and magnetic field components, durations), the causal relationship is unproven and may just as likely be the result of artifacts inherent in this type of analysis.

REFERENCE:
Lilienfeld, A.M. and D.E. Lilienfeld
FOUNDATIONS OF EPIDEMIOLOGY
2nd Edition, Oxford University Press, New York, Oxford (1980)

***

MILHAM

/

CARCINOGENIC
CHRONIC
CYTOGENETIC
EPIDEMIOLOGIC
HUMAN
IN-VIVO
MODULATED
MORTALITY
MUTAGENIC
OCCUPATIONAL
RFR

//

1982
0
0
0
0

///

93
Smialowicz, R.J., M.M. Riddle, C.M. Weil, P.L. Brugnolotti, and J.B. Kinn
ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHZ RADIO FREQUENCY RADIATION (Brief Communication)
Bioelectromagnetics, Vol. 3, No. 4, pp. 467-470 (1982c)

*

AUTHOR ABSTRACT: Groups of female BALB/C mice were irradiated with 425-MHz radio frequency (RF) radiation either continuous wave (CW) or pulse modulated (PM, 1-ms pulse width, 250 pulses/s). Mice were irradiated in a rectangular strip-transmission line at average forward powers of 78, 17.7, or 5 W for CW and 17.7, 5, or 1.25 W for PM. The mean specific absorption rate, as measured using twin-well calorimetry was 7.7 W/kg for a forward power of 70 W. No differences in the mitogen-stimulated response of lymphocytes or in the primary antibody response to sheep erythrocytes or polyvinylpyrrolidone were observed between irradiated and sham-irradiated mice, nor between mice exposed to either CW or PM 425-MHz RF radiation.

**

Study Type: Immunology and Hematology; IN VIVO; MOUSE
Effect Type: Alteration of: response to immunization with sheep erythrocytes or polyvinylpyrrolidone, peripheral blood counts, or mitogen-stimulated lymphocyte responses to CW or pulsed RFR
Frequency: 425 MHz
Modulation: CW or 1-ms pulses at 250 pps (0.25 duty cycle)
Power Densities: Not specified; forward power of 5, 17.7, or 78 W for CW or 1.25, 5, or 17.7 W Av for pulsed
SAR: 0.14, 0.55, 1.9, or 8.6 W/kg for forward power of 1.25, 5, 17.7, or 78 W

EXPOSURE CONDITIONS: Mice confined in small individual containers were exposed concurrently in groups of 4 within a TEM cell at 22 deg C for 1 hr/day on 5 consecutive days to 425-MHz CW or pulsed RFR. Although the exposure chamber was a TEM cell, the presence of the TE01 mode at 425 MHz was detected, so the RFR was not plane wave (Smialowicz et al., 1982a). Equal numbers of mice were sham-exposed concurrently.

OTHER INFORMATION: The whole-body SAR of each mouse in the 4 positions within the TEM cell in the presence of the others was determined at 70 W forward power by twin-well calorimetry. There were no statistically significant differences among the values for the 4 positions. The group average SAR was 7.7 W/kg with a standard deviation of 1.8 W/kg.

Immediately after the last exposure session, groups of mice were immunized with sheep red blood cells (SRBC). Four days later, the spleens were removed and assayed for anti-SRBC antibodies by the direct plaque-forming-cell (PFC) method. The results, expressed as mean log

PFC/spleen (Table 1) showed no significant differences between RFR- and sham-exposed groups or between CW- and pulsed-RFR groups. Other groups of mice exposed to CW or pulsed RFR at 17.7 W (1.9 W/kg) were immunized with polyvinylpyrrolidone (PVP), and 5 days later, their spleens were assayed for PFC with PVP-coated SRBC. Again, no significant differences were found (data not presented).

Erythrocyte count (RBC), leukocyte count (WBC), hematocrit, hemoglobin concentration, and the differential counts of lymphocytes, monocytes, eosinophils, and polymorphonuclear leukocytes in peripheral blood of other mice were determined immediately after the last RFR- or sham-exposure. The results for exposure to CW RFR at 78 W (8.6 W/kg) and to pulsed RFR at 17.7 W (1.9 W/kg) (Table 2) showed that the only significant differences ($p < 0.05$, analysis of variance) were for the CW groups: the mean WBC and mean absolute lymphocyte count were both higher for the RFR than the sham-exposed mice. A multivariate analysis of variance of the hemograms revealed no difference between the CW- and pulsed-RFR groups. However, the mean WBC and mean lymphocyte count for the sham-CW group were significantly lower than for the sham-pulsed group.

Spleen-cell suspensions prepared 24 hr after the last exposure to CW- or pulsed RFR at 17.7 W (1.9 W/kg) were stimulated with the mitogens phytohemagglutinin (PHA), concanavalin A (Con A), E. coli lipopolysaccharide (LPS), or pokeweed (PWM) at several concentrations and assessed for lymphocyte responsiveness. There were no significant differences in responsiveness between RFR- and sham-exposed groups or between CW- and pulsed-RFR groups (no data presented).

CRITIQUE: Although some of the data were not presented in this brief communication, the results of this investigation showed no effects of 425-MHz CW or pulsed RFR on the immune system of the mouse at SARs from 0.14 to 8.6 W/kg. These negative findings support the results for similar immunological parameters in mice perinatally exposed to 425-MHz CW RFR at SARs from 11.3 to 20.6 W/kg (Smialowicz et al., 1982b).

The finding of no in vivo RFR-induced differences in in vitro mitogen-stimulated splenic-lymphocyte cultures from mice is at variance with positive results for rats exposed to 425-MHz CW RFR (Smialowicz et al., 1982a), but the investigators reported large variabilities among rats and between similar experiments, so the latter findings were inconclusive. Moreover, the validity of comparing immunological results in mice and rats is open to question.

REFERENCES:
Smialowicz, R.J., C.M. Weil, J.B. Kinn, and J.A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a)

Smialowicz, R.J., M.M. Riddle, R.R. Rogers, and G.A. Stott
ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 121-126 (1982b)

***

SMIALOWICZ
RIDDLE
WEIL
BRUGNOLOTTI
KINN

/

ANTIBODY
ANTIGEN
CW
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LYMPHOCYTE
MITOGEN
MOUSE
PULSED
RFR

//

1982
425
0.25-1
0
0.14-8.6

///

94
Smialowicz, R.J., M.M. Riddle, R.R. Rogers, and G.A. Stott
ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 121-126 (1982b)

*

AUTHOR ABSTRACT: Groups of time-bred pregnant mice were irradiated with 2450-MHz microwaves at an incident power density of 28 mW/sq cm for 100 min daily from day 6 to 18 of pregnancy. The average specific absorption rate (SAR) was 16.5 W/kg. Two experiments were performed under these conditions. At 3 and 6 weeks of age the mice were assessed for development of the primary immune response to sheep erythrocytes, in vitro mitogen-stimulated lymphocyte proliferation, and natural killer (NK) cell activity. No consistent significant difference in the primary immune response, in the mitogen response, or in the NK cell activity was observed between irradiated and sham-irradiated mice.

**

Study Type: Immunology and Hematology, Physiology and Biochemistry; IN VIVO; MOUSE
Effect Type: Alterations of litter size and weight and of immune system development in neonate mice exposed to RFR in utero
Frequency: 2.45 GHz
Modulation: CW
Power Densities: 28 mW/sq cm
SAR: 16.5 W/kg

EXPOSURE CONDITIONS: Pregnant mice were exposed in 5 X 5 arrays for 100 min/day on gestational days 6 through 18 to far-field 2.45-GHz CW RFR at 28 mW/sq cm (SAR of 16.5 W/kg) in an anechoic chamber at 50% relative humidity and temperature of 22.0 deg C (first experiment) or 20.2 deg C (second experiment). Control mice were sham-exposed.

OTHER INFORMATION: From Berman et al. (1978), the SAR at 10 mW/sq cm varied with position in the 5 X 5 array from 4.05 to 7.37 W/kg with an array mean of about 5.9 W/kg; the corresponding values at 28 mW/sq cm ranged from about 11.3 to 20.6 W/kg with a mean of 16.5 W/kg. The latter value is more than twice the basal metabolic rate of a mouse (6.4 W/kg).

On the morning after birth, live and dead neonates were counted and weighed, and the mean litter weight was determined. At age 6 days, the number of live neonates and the mean litter weight were ascertained again, and the litters were normalized to 4 pups/litter. Such data were reported for only 6-day-old litters born on gestational day 20 (Table 1). There were no significant differences between RFR- and sham-exposed groups in mean number of live (6-day-old) mice for experiments 1 and 2 (exposures at 22.0 or 20.2 deg C, respectively) or in mean litter weight for experiment 1. The mean litter weight of the RFR-exposed group in

experiment 2 was reported as significantly lower ($p<0.01$, analysis of variance) than of the sham-exposed group.

Immune system development was assessed in 2 pups/litter at age 3 weeks and in the other 2 pups/litter at age 6 weeks, as described below.

Responses of splenic-cell cultures to the mitogens phytohemagglutinin (PHA), concanavalin A (Con A), pokeweed (PWM), and E. coli lipopolysaccharide (LPS) were determined by assaying the uptake, in DNA, of tritiated thymidine added to the cultures 72 hr before harvesting. The counts per min (CPM) were log-transformed and analyzed with Student's t-test. Only the data for optimal concentration of each mitogen were presented (Table 3). For the age 3- and 6-week mice in experiment 1 and the 6-week mice in experiment 2, there were no significant differences ($p<0.05$), between RFR- and sham-exposed groups, of thymidine uptake in cultures stimulated with any of the mitogens. (Such assays were not done for the 3-week-old mice in experiment 2.) The only significant difference was between the unstimulated cultures for the 6-week-old mice in experiment 1; the uptake was smaller for the RFR-exposed group than for the sham-exposed group. The corresponding difference in experiment 2 was of opposite sign but nonsignificant.

At each age, the primary antibody response of mice was determined by immunizing them with sheep red blood cells (SRBC) and assaying the spleens 4 days later for IgM anti-SRBC antibodies by determining the numbers of plaque-forming cells (PFC). The results were expressed as mean numbers of PFC per million spleen cells and per spleen. Only the results for the 6-week-old mice were presented (Table 2). The differences between RFR- and sham-exposed groups for either quantity in experiment 1 were not significant. In experiment 2, the number of PFC per million spleen cells for the RFR-exposed group was larger than for the sham-exposed group at the barely significant ($p = 0.05$) level, but the difference in the number of PFC per spleen was not significant. Serum hemolysin and hemagglutination titers were also determined; no significant differences were found (data not presented).

Spleen cells were assayed for natural-killer (NK) cell activity against subline YAC-1 lymphoma cells in vitro. Cultures of YAC-1 cells were radiolabeled with Cr-51, added to graded numbers of splenic effector cells, and incubated for 4 hr at 37 deg C. After centrifugation, the supernatant was assayed, with a gamma counter, for E, the Cr-51 released from the target cells in the presence of the spleen cells. Spontaneous Cr-51 release, S, was ascertained from labeled cultures of YAC-1 cells in the absence of spleen cells. Maximum Cr-51 release, T, was determined by adding Triton X-100 to cultures of labeled YAC-1 cells. Both E and T were corrected for spontaneous radioactivity by subtracting S. The results (Table 4) for various ratios of effector (spleen) cells to target (YAC-1) cells were expressed as percentages:

$$100(E - S)/(T - S).$$

There were no significant differences between RFR- and sham-exposed groups in NK-cell activity at any ratio for the 3-week-old mice in experiments 1 and 2 or for the 6-week-old mice in experiment 1. For the 6-week-old mice in experiment 2, NK-cell activity for the RFR group was lower than for the sham group for all three effector-cell/target-cell ratios used (25:1, 50:1, 100:1), with the difference for 50:1 labeled as significant ($p<0.05$, t-test). (However, calculations show that the difference for 50:1 was nonsignificant, but that the difference for 100:1 was significant.)

CRITIQUE: Although the text states that the mean litter weight of the RFR-exposed group in experiment 2 was significantly lower ($p<0.01$) than for the corresponding sham-exposed group, a calculation for the data in Table 1 shows that the difference was nonsignificant ($p>0.05$). Thus, contrary to the discussion by the investigators, these results do not support the weight decreases reported by Berman et al. (1982) (referenced as "in press, 1981"). It is interesting to note that the mean litter weight for the sham-exposed mice was significantly lower in experiment 2 than in experiment 1 (a non-RFR effect), which may have influenced other differences in results between two experiments.

As indicated by the investigators, the absence of in vivo RFR-induced alterations of in vitro stimulation of mouse lymphocytes by any of the mitogens is at variance with the increased mitogen responses in rat lymphocytes from prenatal exposure to 2.45 GHz (Smialowicz et al., 1979a) or 425-MHz RFR (Smialowicz et al., 1982a) (the latter referenced as "submitted for publication, 1981b"). However, the findings of the latter investigation were inconclusive because of the large variabilities in the in vitro mitogen-stimulated responses among rats and between similar experiments. Moreover, the validity of comparing immunological results in mice and rats is open to question. Lastly, in another presumably subsequent investigation, Smialowicz et al. (1982c) again found no significant differences in mitogen-stimulated lymphocyte responses for mice exposed to 425-MHz CW- or pulsed RFR at SARs from 0.14 to 8.6 W/kg.

Regarding the cultures not stimulated with mitogens, again it is interesting that the mean thymidine uptake for the 6-week-old sham-exposed mice in experiment 1 was significantly larger than for the sham-exposed mice in experiment 2. Exposure to RFR evidently did not alter the response to SRBC immunization. However, because the values of NK-cell activity for the 6-week-old RFR-exposed groups were all lower than for their corresponding sham-exposed groups, the results are indicative of a possible RFR-induced effect even though only one of the six differences was statistically significant. Repetition of such experiments would be necessary to confirm or deny the existence of this effect.

REFERENCES:

Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978)

Berman E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982)

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Smialowicz, R.J., C.M. Weil, J.B. Kinn, and J.A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a)

Smialowicz, R.J., M.M. Riddle, C.M. Weil, P.L. Brugnolotti, and J.B. Kinn
ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHZ RADIO FREQUENCY RADIATION (Brief Communication)
Bioelectromagnetics, Vol. 3, No. 4, pp. 467-470 (1982c)

***

SMIALOWICZ
RIDDLE
ROGERS
STOTT

/

ANTIBODY
ANTIGEN
BIOCHEMISTRY
CW
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MITOGEN
MOUSE
PHYSIOLOGY
RFR
TRACER
WEIGHT

//

1982
2450
1
28
16.5

///

95
Smialowicz, R.J., P.L. Brugnolotti, and M.M. Riddle
COMPLEMENT RECEPTOR POSITIVE SPLEEN CELLS IN MICROWAVE (2450-MHZ)-IRRADIATED MICE
J. Microwave Power, Vol. 16, No. 1, pp. 73-77 (1981c)

*

AUTHOR ABSTRACT: Male CBA/J mice were exposed under far-field conditions in a temperature and humidity controlled environment to 2450-MHz (CW) microwaves. Mice were exposed once for 30 minutes at a power density of 15, 20, 30, or 40 mW/sq cm. The whole-body-averaged dose rate was approximately 0.7 mW/g per mW/sq cm. Six days after irradiation, the percentage of complement-receptor-positive (CR+) spleen cells was determined. No difference was observed in the percentages of CR+ spleen cells of young adult (10-12-week-old) mice exposed at any of the power densities as compared with sham-irradiated controls. However, a significant ($P < 0.05$) increase was observed in the percentage of CR+ cells from 16-week-old mice exposed at 40 mW/sq cm. This increase in CR+ cells was accompanied by a significant ($P < 0.05$) decrease in the number of nucleated cells in the spleens of these mice. This change in CR+ and nucleated spleen cells was not consistently produced. The available data indicate that the age and strain of the mouse, the microwave exposure characteristics, and the environmental conditions may all be sources of variation that affect the CR+ end point.

**

Study Type: Immunology and Hematology; IN VIVO; MOUSE
Effect Type: RFR-induced increases in percentage of splenic complement-receptor-positive (CR+) cells
Frequency: 2.45 GHz
Modulation: CW
Power Densities: 15, 21, 30, or 40 mW/sq cm
SAR: 11, 14, 22, or 29 W/kg

EXPOSURE CONDITIONS: Mice individually housed in foamed-polystyrene cages were exposed for 30 min to far-field RFR at 15, 20, 30, or 40 mW/sq cm in groups of 4 in a diamond array under a horn in an anechoic chamber maintained at 24 deg C and 50% relative humidity. Control mice were sham-exposed under the same conditions.

OTHER INFORMATION: CBA/J mice were used rather than the BALB/c strain in a previous investigation because Schlagel et al. (1980) had reported RFR-induced increases of CR+ cells for 12-week-old CBA/J (H-2k haplotype) but not BALB/c (H-2d haplotype) mice.

Mice 10-12 weeks old were sham-exposed or exposed for 30 min to the RFR at 15, 20, 30, or 40 mW/sq cm (8 mice per level). Six days after treatment, the spleens were removed and assayed for percentages of CR+ cells by rosette formation with sheep erythrocytes. Lymphocytes having 3 or more adherent erythrocytes were scored as CR+ cells. Small,

nonsignificant ($p>0.05$) decreases or increases in the mean percentage of CR+ cells were obtained. The investigators noted that the SAR corresponding to 20 mW/sq cm (14 W/kg) was approximately the same as that used by Wiktor-Jedrzejczak et al. (1977) and that the SARs for 15 and 30 mW/sq cm (11 and 22 W/kg) were within the range used by Sulek et al. (1980), who reported significant increases of CR+ cells. Smialowicz et al. (1981c) also noted that the mice exposed at 40 mW/sq cm were visibly under thermal stress. (They indicated that in another experiment, 6 of 25 mice died during or soon after completion of exposure at 40 mW/sq cm for 60 min.)

Under the hypothesis that older mice may be more susceptible to the effect sought, 16-week-old mice were then exposed for 30 min at 40 mW/sq cm (SAR not stated). The results indicated a significant ($p<0.001$) increase in percentage of CR+ cells, but also a barely significant ($p<0.05$) decrease of nucleated cells in the spleen. The investigators suggested that the results may be indicative of a redistribution of CR+ cells to the spleen or of a shift in spleen-cell population related to thermal stress, in consonance with the findings of Lotz and Michaelson (1978) in the rat and of Liburdy (1979, 1980) in the mouse. However, Smialowicz et al. (1981c) obtained negative results for 14-week-old mice at 40 mW/sq cm and for 24-week-old mice (retired breeders) at 40 and 30 mW/sq cm.

Smialowicz et al. (1981c) expressed difficulty in reconciling their negative results with the positive results (all from another laboratory) of Wiktor-Jedrzejczak et al. (1977), Schlagel et al. (1980), and Sulek et al. (1980). Smialowicz et al. (1981c) speculated that their far-field exposure system may have produced vastly different internal SAR distributions in the mouse (for equivalent whole-body SARs) than the waveguide exposure system used by the other investigators.

CRITIQUE: As indicated by Smialowicz et al. (1981c), the use of a different kind of exposure system than that used by the other investigators may have been an important factor in the contradictory findings of the two laboratories. In a far-field system, the electric and magnetic components are both transverse to the propagation direction. However, in a waveguide system operated in the TE01 mode, the electric vector is transverse to the propagation direction but the magnetic vector has components both parallel (longitudinal) and transverse to the propagation direction. Additional research would be needed to ascertain whether the presence of the longitudinal magnetic-field component is a major contributor to the differences in findings.

Smialowicz et al. (1981c) used male CBA/J mice, whereas the sex of the CBA/J mice used by Schlagel et al. (1980) and Sulek et al. (1980) was not stated. On the other hand, Wiktor-Jedrzejczak et al. (1977) also used male CBA/J mice, so it is unlikely that the sex of the mice was a contributory factor.

It is possible that there were subtle but important differences in the apparently similar methodology used by both laboratories for removing and assaying the spleens for CR+ cells. Again, further research would be necessary to explore this possibility.

REFERENCES:

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)

Lotz, W.G. and S.M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHIPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol: Respirat. Environ. Exercise Physiol.,
Vol. 44, No. 3, pp. 438-445 (1978)

Schlagel, C.J., K. Sulek, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE. II. STUDIES ON THE MECHANISMS CONTROLLING SUSCEPTIBILITY TO MICROWAVE-INDUCED INCREASES IN COMPLEMENT RECEPTOR-POSITIVE SPLEEN CELLS
Bioelectromagnetics, Vol. 1, No. 4, pp. 405-414 (1980)

Sulek, K., C.J. Schlagel, W. Wiktor-Jedrzejczak, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980)

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977)

***

SMIALOWICZ
BRUGNOLOTTI
RIDDLE

/

ANTIGEN
COMPLEMENT
CW
IMMUNOLOGY
IN-VIVO
MOUSE
LEUKOCYTE
LYMPHOCYTE
RFR
STRESS

//

1981
2450
1
15-40
11-29

///

96.
Schlagel, C.J., K. Sulek, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE. II. STUDIES ON THE MECHANISMS CONTROLLING SUSCEPTIBILITY TO MICROWAVE-INDUCED INCREASES IN COMPLEMENT RECEPTOR-POSITIVE SPLEEN CELLS
Bioelectromagnetics, Vol. 1, No. 4, pp. 405-414 (1980)

*

AUTHOR ABSTRACT: In attempting to evaluate the mechanisms responsible for susceptibility to the inductive increase in splenic complement receptor-positive (CR+) cells following exposure to 2450-MHz microwaves, it was found that sensitivity to microwave-induced CR+ cell increases was under genetic control. In particular, evidence was accumulated suggesting that regulation was under the control of a gene or genes closely associated with but outside of the mouse major histocompatibility complex (H-2). All responsive strains of mice tested were of the H-2k haplotype, while mice of the H-2a, H-2b, H-2d and H-1i5 haplotypes were refractory to the microwave-induced increases in CR+ cells.

By utilizing certain H-2k strains of mice that were genetically unable to respond to endotoxin, we were able to show that these strains of mice responded to microwaves, but not to endotoxin, by increasing CR+ cells. Microwave-induced increases in CR+ cells were not mimicked by the intraperitoneal injection of hydrocortisone. Athymic mice responded to microwave exposure, indicating that this event was not regulated by the T-cell population. Mice less than eight weeks old were found not to be susceptible to exposure to 2450-MHz microwaves.

These studies indicate that microwaves do induce changes in the population of cells with specific cell-surface receptors, that susceptibility to these changes is under genetic control, and that it is unlikely that endotoxin, corticosteroids, or regulatory T cells play a significant role in the mechanisms regulating these increases.

**

Study Type: Immunology and Hematology; IN VIVO; MOUSE
Effect Type: Genetic factors in the susceptibility to RFR-induced increases in mouse spleen cells having complement receptor (CR+ cells)
Frequency: 2.45 GHz
Modulation: CW
Power Densities: Not given; 0.6 W forward power in waveguide
SAR: 9.3 to 19.3 W/kg, depending on age and strain

EXPOSURE CONDITIONS: Mice restrained in polystyrene holders were exposed individually at 0.6 W forward power for 30 min in a waveguide system at 24 deg C, 50% relative humidity, and 6.4 m/min air flow.

OTHER INFORMATION: In initial experiments, CBA/J mice (6 per group) at ages 3, 4, 6, 12, and 30 weeks were individually exposed to 2.45-GHz RFR for 30 min, and equal numbers were sham-exposed. On day 3 and 6 after treatment, the spleens were removed and assayed for percentages of complement-receptor-positive (CR+) cells by rosette formation with sheep red blood cells. A lymphocyte having 3 or more adherent erythrocytes was scored as a positive rosette. From Table 1, the assays on day 3 for the 12- and 30-week old mice showed significantly higher percentages of CR+ cells than for the sham-exposed mice, and the differences for the younger mice were nonsignificant; the assays on day 6 showed higher percentages for the 6- and 12-week-old mice, but not for the younger or 30-day-old-mice. Thus, 12-week-old mice were used in subsequent experiments with other strains.

The ontogeny of CR+ cells is under the control of at least 2 genes, one of which is closely linked to the H-2 region. Therefore, the possibility that the RFR-induced increases of CR+ cells were associated with the H-2 haplotype was investigated. From Table 2, there were no RFR-induced significant increases of CR+ cells on assay day 3 for mice bearing the H-2a, H-2b, or H-2d haplotypes; similar results were obtained on assay day 6 for all of these strains except for DBA/2(d), which did show a significant increase of CR+ cells. By contrast, many (but not all) of the strains bearing the H-2k haplotype showed significant increases of CR+ cells on both assay days. Among the strains that yielded such RFR-induced increases were CBA/N and C3H/HeJ, which are known to possess genetic defects that alter their responsiveness to injection with lipopolysaccharide (LPS).

To test whether the observed increases of CR+ cells were due to RFR-induced in-situ release of endotoxin, groups of these and two other strains (CBA/J and C57BL/6) were either exposed to the RFR for 15 or 30 min or were injected with either of two doses of LPS; sham-exposed and uninjected groups served as respective controls. The spleens of all mice so treated were assayed on day 3, 6, or 9. From Table 3 (for assay day 6), the CBA/J and the CBA/N mice showed significant RFR-induced increases of CR+ cells; the increases from LPS injection of these two strains were labeled by the investigators as significant at the $p<0.01$ level, but t-test calculations show that the increases were not significant ($p>0.05$).

RFR-exposure of the C3H/HeJ mice for 30 min yielded increases of CR+ cells that were labeled as significant, but were not significant, and the increases due to RFR exposure of the C57BL/6 mice or to injection of LPS in the C3H/HeJ mice were also nonsignificant. However, significant increases were obtained in the C57BL/6 mice with either dose of LPS. Thus, there was no correlation between the susceptibility to RFR-induced and LPS-induced increases of CR+ cells. Similar experiments involving injection of hydrocortisone (HC) at either of two doses were performed. The results (Fig. 1) indicated that either dose of HC produced marked depression of CR+ cells in CBA/J mice on assay day 3, and return to normal values on day 6. The investigators concluded that endotoxin or corticosteroids are unlikely to be involved in the observed RFR-induced increases of CR+ cells.

Athymic nude mice of the CBA/H T6J nu/nu strain, which lack mature T cells, were exposed to the RFR. The results (Table 2) showed increases of CR+ cells comparable to those for the RFR-exposed CBA/J mice, so such increases in the latter strain are not regulated by the T-cell population.

CRITIQUE: As in other papers from this group (Wiktor-Jedrzejczak et al., 1977; Sulek et al., 1980), there appear to be several discrepancies between statements by the investigators regarding statistical significance and t-test calculations with the data presented. Two such discrepancies were noted above, and others can be discerned from the data in Tables 1-3. However, none of these discrepancies, if real, would materially alter the qualitative conclusions of the investigators, which were that: (1) significant increases in percentages of splenic CR+ cells were induced by RFR exposure in mouse strains only bearing the H-2k haplotype (but not in all such strains tested), thus indicating that the susceptibility to this effect is related to genetic factors; (2) such increases were unlikely to be due to RFR-induced release of endotoxin or corticosteroids; and (3) such increases (in normal strains) are not regulated by the T-cell population.

The importance of the dependence of this RFR-induced effect on genetic factors with regard to possible analogous effects in other species (particularly humans) is unknown. However, in the last sentence of their discussion, the investigators characterized the increase in CR+ cells in CBA/J mice (Sulek et al., 1980) as a nonthermogenic response to RFR exposure. This point is questionable, in view of the whole-body SARs involved.

It should be noted for reasons not yet clear, Smialowicz et al. (1982c) were unable to reproduce the positive findings above with CBA/J mice.

REFERENCES:

Smialowicz, R.J., P.L. Brugnolotti, and M.M. Riddle
COMPLEMENT RECEPTOR POSITIVE SPLEEN CELLS IN MICROWAVE (2450-MHZ)-IRRADIATED MICE
J. Microwave Power, Vol. 16, No. 1, pp. 73-77 (1981c).

Sulek, K., C.J. Schlagel, W. Wiktor-Jedrzejczak, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980)

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977)

***

SCHLAGEL
SULEK
HO
LEACH
AHMED
WOODY

/

CW
COMPLEMENT
CORTICOSTEROID
CYTOGENETIC
HAPLOTYPE
IMMUNOLOGIC
IN-VIVO
LYMPHOCYTE
MITOGEN
MOUSE
RFR

//

1980
2450
1
0
9.3-19.3

///

97
Liddle, C.G., J.P. Putnam, J.S. Ali, J.Y. Lewis, B. Bell, M.W. West, and O.H. Lewter
ALTERATION OF CIRCULATING ANTIBODY RESPONSE OF MICE EXPOSED TO 9-GHZ PULSED MICROWAVES
Bioelectromagnetics, Vol. 1, No. 4, pp. 397-404 (1980)

*

AUTHOR ABSTRACT: A significant increase was observed in the circulating antibody titers of mice exposed to 9-GHz pulsed microwaves at an average power density of 10 mW/sq cm, two hours per day for five days compared with sham-irradiated animals. The mice were previously immunized with type III pneumococcal polysaccharide. Following irradiation, a portion of the immunized animals were challenged with virulent Streptococcus pneumoniae, type III. Ten days after challenge, mortality was essentially the same in the two groups, but during the ten day period, there was a noticeable increase in the survival time of the irradiated animals compared with the sham-irradiated animals, suggesting that the increased circulating antibody response afforded some degree of temporary protection to the animals.

**

Study Type: Immunology and Hematology; IN VIVO; MOUSE
Effect Type: RFR-induced changes in circulating antibody titers and in response to challenge with Streptococcus pneumoniae of mice previously immunized with a killed bacterin of type III S. pneumoniae or with type III purified pneumococcal polysaccharide
Frequency: 9.0 GHz
Modulation: Pulsed: 1-microsecond pulses at 970-1000 pps
Power Densities: 10 mW/sq cm Av; 10 W/sq cm Pk
SAR: 3.3-4.7 W/kg (calculated)

EXPOSURE CONDITIONS: Mice in individual plastic containers were exposed to far-field RFR in groups of 4 for 5 days, 4 hr/day, in an anechoic chamber at constant temperature, relative humidity, and air flow rate. Other groups of 4 mice were sham-exposed.

OTHER INFORMATION: Initial blood samples of female CD-1 mice 28-35 days old were analyzed for red and white blood cell counts, hematocrit, and hemoglobin, and differential leukocyte counts were made. One week later, 6 groups of 4 mice were immunized by injection with a killed bacterin of Streptococcus pneumoniae type III, and other groups were immunized by injection of type III purified pneumococcal polysaccharide (PPS). Still another group was injected with equal quantities of saline, to serve as cage controls. Each group (except the cage controls) was then either sham-exposed or exposed to pulsed 9-GHz RFR at an average power density of 10 mW/sq cm for 5 days, 2 hr/day. Calculated SARs were 3.3 W/kg for a multilayered spherical model and 4.7 W/kg for a prolate spheroid model. Rectal temperatures were taken just before and after treatment on the second day.

On the day after completion of treatment (day 6 after immunization), blood samples were analyzed for hemagglutination with sheep red blood cells and for hematology. In addition on that day, the mice were challenged with an injection of an LD50 dose of virulent S. pneumoniae type III, and day of death was recorded for 10 days after challenge. The saline-injected controls were similarly challenged.

The hemagglutination titers for the RFR-exposed mice were significantly higher (28%) than for the sham-exposed mice. No antibody titers were detected in the saline-injected controls. Within the 10 days after challenge, 47.2% (25/53) of the RFR-exposed and 50.0% (27/54) of the sham-exposed mice had died; the difference was statistically nonsignificant. None of the saline-injected (nonimmunized) controls survived the challenge. The last death in the RFR-exposed mice occurred on day 7, and it occurred on day 6 in the sham-exposed mice. Also, the greatest number of deaths in one day for the RFR-exposed mice occurred on day 6 after challenge (10 mice), whereas for the sham-exposed mice it occurred on day 3 (14 mice). The mean day of death was 5.58 +/- 1.61 (SD) for the RFR-exposed mice and 4.78 +/- 1.37 for the sham-exposed mice; use of the Mann-Whitney U test yielded p = 0.073 for the difference.

There were no significant differences in erythrocyte and leukocyte counts, differential leukocyte counts, hemoglobin values, or hematocrits between the RFR- and sham-exposed mice.

Rectal temperature measurement yielded a mean increase of 0.08 +/- 0.59 deg C for the RFR-exposed mice and a mean decrease of 0.02 +/- 0.72 deg C for the sham-exposed mice; the difference was not statistically significant.

The investigators surmized that the higher antibody titers in the RFR-exposed mice was an indication of increased protection against S. pneumoniae, a conjecture supported by the longer survival time of these mice, so the nonsignificant difference in total-mortality percentages for the RFR- and sham-exposed mice was unexpected. The investigators suggested that the higher levels of circulating antibodies in the RFR-exposed mice afforded some initial neutralization of the antigen, but not enough to ensure recovery.

CRITIQUE: The longer survival times of the RFR-exposed mice are qualitatively similar to an incidental observation of Prausnitz and Susskind (1962) that mice exposed to 9.3-GHz pulsed RFR at 100 mW/sq cm average power density for 59 weeks, 4.5 min/day, seemed to have greater resistance than controls to a pneumonia infection accidentally introduced into their colony. Similarly, Pautrizel et al. (1975) reported that exposure of mice to RFR (frequency and intensity not specified) conferred protection against an otherwise fatal challenge with Trypanosoma equiperdum.

The nonsignificant rectal temperature changes observed by Liddle et al. (1980) may indicate that the mice were not subjected to appreciable thermal stress. It could be hypothesized that the mice were stressed by perception of the RFR as apparent sound in the head (Frey, 1961) or as actual sound from pulse impact on the structures housing the mice during exposure (White, 1963), or both, because the RFR consisted of 1-microsecond pulses of 10 W/sq cm peak power density. This speculation appears to be untenable because in a subsequent abstract, Liddle et al. (1982) indicated that mice immunized against S. pneumoniae and exposed to 2.45-GHz CW RFR at 10 mW/sq cm, which would not give rise to the RFR-auditory effect, survived a subsequent challenge longer than sham-exposed immunized mice. They also found that survival rates of both RFR- and sham-exposed mice increased when the ambient temperature during treatment was raised. However, the SAR at this frequency and power density was 6.8 W/kg, i.e., considerably higher than at 9 GHz.

REFERENCES:

Frey, A.H.
AUDITORY SYSTEM RESPONSE TO RADIO-FREQUENCY ENERGY
Aerospace Med., Vol. 32, pp. 1140-1142 (1961)

Liddle, C.G., J.P. Putnam, and O.H. Lewter
ENHANCED SURVIVAL OF MICE EXPOSED TO MICROWAVES FOLLOWING INFECTION WITH STREPTOCOCCUS PNEUMONIAE
Abstract of Bioelectromagnetics Symposium, Los Angeles, CA, p. 88 (June-July 1982)

Pautrizel, R. et al.
STIMULATION OF THE DEFENSES OF MICE WITH TRYPANOSOMIASIS BY EXPOSURE TO RADIATION ASSOCIATED WITH A MAGNETIC FIELD AND ELECTROMAGNETIC WAVES
Compt. Rend. D., Vol. 280, pp. 1915-1918 (1975)

Prausnitz, S. and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)

White, R.M.
GENERATION OF ELASTIC WAVES BY TRANSIENT SURFACE HEATING
J. Appl. Phys., Vol. 34, pp. 3559-3567 (1963)

***

LIDDLE
PUTNAM
ALI
LEWIS
BELL
WEST
LEWTER

/

ANTIBODY
ANTIGEN
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
MORTALITY
MOUSE
PULSED
RECTAL
RFR

//

1980
9000
0.001
10
3.3-4.7

///

98
McRee, D.I., R. Faith, E.E. McConnell, and A.W. Guy
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: EVALUATION OF HEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 45-52 (1980)

*

AUTHOR ABSTRACT: Four rabbits were sham-exposed and four were exposed to 2450-MHz CW radiation for six months. Daily duration of exposure was 23 h and continued across 180 consecutive days. The rabbits were exposed at the University of Washington by Dr. Arthur W. Guy. A companion paper to this one provides details of the method used to expose the animals. The power density at the body axis of the animals was 7 mW/sq cm and at the head location, 10 mW/sq cm. The measured peak specific absorption rate (SAR) in the head was 17 W/kg, and the maximum average whole-body SAR as determined from calculations assuming a prolate spheroid geometry was 1.5 W/kg.

Blood samples were drawn for hematologic and serum-chemistry analyses immediately after termination of exposure. Eosinophil percentage, albumin and calcium levels were significantly lower in exposed than in control rabbits. Thirty days after termination of exposure no change in hematological parameters was observed, but a significant decrease in albumin/total globulin ratio was measured in the exposed animals.

The animals were euthanized thirty days after termination of exposure. No pathologic differences were detected in tissue samples. Analysis of bone marrow from the sternum showed a significant increase in the myeloid/erythroid ratio in the exposed animals. Splenic lymphocytes were stimulated by three different mitogens: phytohemagglutinin, concanavalin A and pokeweed. Lymphocytes from exposed animals showed a significant suppression in responsiveness to pokeweed mitogen.

**

Study Type: Immunology and Hematology, Physiology and Biochemistry; IN VIVO; RABBIT
Effect Type: RFR-induced alterations of hematology, histology, and splenic lymphocytes stimulated with mitogens
Frequency: 2.45 GHz
Modulation: CW
Power Density: 10 mW/sq cm
SAR: 17 W/kg (max) in the head (measured); 1.5 W/kg whole body (calculated)

EXPOSURE CONDITIONS: Four rabbits housed in acrylic cages were concurrently exposed dorsally in individual anechoic chambers to 2.45-GHz CW RFR 23 h/day for 180 days in the far field of a horn in each chamber. The electric vector was parallel to the long axis of the rabbit. Four other rabbits were sham-exposed in similar chambers concurrently with the RFR-exposed rabbits. The 8 chambers were maintained at 24 deg C by a common air conditioner.

OTHER INFORMATION: RFR- and sham exposures of the 8 rabbits and the dosimetry were done in another laboratory (see Guy et al., 1980b). Use of thermography on rabbit carcasses indicated that for 10 mW/sq cm at the location of the head, the peak SAR in the head was 17 W/kg. By calculation for a prolate spheroidal model of a rabbit exposed to 2.45-GHz RFR at 10 mW/sq cm, the whole-body SAR is about 1.5 W/kg.

Blood samples taken immediately after completion of the 180-day RFR- or sham exposures were analyzed for hematologic and clinical-chemistry parameters. A two-sided Mann-Whitney U-test was used to evaluate differences for significance. The levels of albumin, calcium, and eosinophils for the RFR-exposed rabbits were reported in the text as significantly lower ($p<0.05$) than for the sham-exposed rabbits, but Table 1 shows that the albumin and calcium levels were higher; only the eosinophil level was lower. There were no significant differences for the remaining parameters. The investigators stated that significant differences for 3 of the 41 parameters measured is close to chance expectation irrespective of treatment, so the validity of these 3 positive findings is open to question. (Table 1 shows only 39 parameters, but the difference does not materially affect this point.) Measurements of catecholamines and creatinine in the urine, also made immediately after completion of exposure, showed no significant differences between the two groups.

Analyses of blood samples taken 30 days after completion of exposure were reported as showing no significant differences between the groups (no data given), i.e., the levels of albumin, calcium, and eosinophils had normalized. The levels of serum proteins were also measured at this time. None of the differences was significant, but a decrease in the albumin and an increase in the total-globulin levels yielded a significantly lower albumin/total-globulin (A/G) ratio for the RFR-exposed group. The A/G ratios for the two groups immediately after exposure termination were essentially the same, so the investigators indicated that the biologic importance of this finding is difficult to interpret and may be negligible.

Thirty days after completion of exposure, the rabbits were euthanized and the lungs, liver, kidneys, adrenals, thyroid, pituitary, brain, and testes were weighed; histopathological analyses were performed on these and various other tissues; and bone-marrow smears were obtained from the sternum. No lesions attributable to RFR exposure were observed and no significant differences in organ masses (absolute or expressed as percentages of body mass) were reported (Table 5). The myeloid/erythroid ratio (the ratio of granulocytes to nucleated-erythrocyte precursors) was significantly higher for the RFR-exposed rabbits. However, the investigators questioned the biological significance of this positive finding because the leukocyte and erythrocyte counts for the two groups did not differ significantly.

Cultures of splenic cells were stimulated with the mitogens phytohemagglutinin (PHA), concanavalin A (Con A), or pokeweed (PWM), each at three concentrations in the ratio 1:2:4. Tritiated thymidine was added 24 hr before the end of the culture period, and the rate of

synthesis of cellular DNA was evaluated by measuring the uptake of the thymidine by liquid scintillation counting. Tritiated thymidine was also added to cultures not stimulated with mitogens, and the "stimulation index" for each mitogen at each concentration was calculated by dividing the mean radioactivity of the stimulated culture by the mean radioactivity of the nonstimulated culture. For all three mitogens at all three concentrations (Figs. 1, 2, and 3), the stimulation indices for the RFR-exposed group were lower than the corresponding values for the sham-exposed group, but only the differences for PWM were statistically significant (at all three concentrations). The investigators concluded that, based on their limited data, exposure to RFR may suppress immunological competence. Specifically, it appears that both T- and B-cell populations were suppressed, since PHA and Con A are predominantly T-cell mitogens and PWM is nonspecific. However, they also stated that the results might have been different if the mitogen studies had been performed sooner than 30 days after completion of exposure.

CRITIQUE: Regarding the hematological tests, only the results obtained immediately after completion of the 6-month treatment period are presented in this paper; the values prior to, and after 1.5, 3, 4.5, and 6 months of treatment are given in Guy et al. (1980b). The latter data show differences not only in pretreatment values between the two groups (a point mentioned by McRee et al. with regard to lymphocyte percentages), but also differences within each group and between the groups during the treatment period. (Whether any of these differences are statistically significant by the nonparametric Mann-Whitney test used by these investigators cannot be ascertained without the original measurements, and the alternative use of a test based on the normal distribution may yield results that are inconsistent with those of the Mann-Whitney test.) Thus, the investigators correctly discount the few apparently positive hematological findings.

In the studies with mitogen-stimulated splenic-cell cultures, note that for the sham-exposed rabbits, the mean stimulation index for PHA (Fig. 1) decreased from about 9 for the lowest concentration to about 7.5 for the two higher (double and quadruple) concentrations; for Con A (Fig. 2) it increased with increasing concentration; and for PWM (Fig. 3), the index decreased almost linearly with increasing concentration. The biological significance of these variations is not clear, except perhaps that the mitogen concentrations used may not have been near optimum. However, similar directional trends with concentration were evident in the corresponding mean stimulation indices for the RFR-exposed group, so intergroup comparisons at each concentration were probably valid.

If the differences, between the RFR- and sham-exposed groups, in the stimulation indices for the T-cell mitogens PHA and Con A, which were statistically nonsignificant, were taken to be biologically nonsignificant, then the differences for PWM (which were significant) would lead to the conclusion that the RFR depressed only the B-cell population. However, because the PHA and Con A indices for the RFR group were lower for all three concentrations of each mitogen, the

investigators ascribed biological credence to these differences, leading to their conclusion that both the T- and B-cell populations were depressed.

By contrast with the results above, Smialowicz et al. obtained negative results with PHA, Con A, PWM, and the B-cell mitogen lipopolysaccharide for rats exposed to 2.45 GHz (1979a), 100 MHz (1981b), or 970 MHz (1981d). Although such contrary results could be ascribed to differences in methodology and species used by the two research groups, it should be noted that Smialowicz et al. performed their mitogen-stimulation tests on cessation of treatment, whereas McRee et al. did their tests 30 days after treatment. With regard to the latter, it is difficult to understand how RFR-induced lymphocyte-population depression could have persisted for so long without manifesting other health effects in the interim.

REFERENCES:

Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b)

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Smialowicz, R.J., J.S. Ali, E. Berman, S.J. Bursian, J.B. Kinn, C.G. Liddle, L.W. Reiter, and C.M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)

Smialowicz, R.J., C.M. Weil, P. Marsh, M.M. Riddle, R.R. Rogers, and B.F. Rehnberg
BIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE OF RATS TO 970-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 2, No. 3, pp. 279-284 (1981d)

***

MCREE
FAITH
MCCONNELL
GUY

/

BIOCHEMISTRY
CHRONIC
CW
HEMATOLOGY
HISTOLOGY
IMMUNOLOGY
IN-VIVO
LYMPHOCYTE
MITOGEN
PHYSIOLOGY
RABBIT
RFR

//

1980
2450
1
10
1.5-17

///

99
Galvin, M.J., D.I. McRee, C.A. Hall, J.P. Thaxton, and C.R. Parkhurst
HUMORAL AND CELL-MEDIATED IMMUNE FUNCTION IN ADULT JAPANESE QUAIL FOLLOWING EXPOSURE TO 2.45-GHZ MICROWAVE RADIATION DURING EMBRYOGENY
Bioelectromagnetics, Vol. 2, No. 3, pp. 269-278 (1981)

*

AUTHOR ABSTRACT: Japanese quail, Coturnix coturnix japonica, eggs were subjected to 2.45-GHz CW microwave radiation at 5 mW/sq cm (SAR=4.03 mW/g) during the first 12 days of embryogeny. Following hatching the exposed embryos, as well as nonexposed controls, were reared to 22 weeks of age. Humoral immune potential, as indicated by comparable anti-CRBC antibody, IgM and IgG, levels at 0, 4, and 7 days postimmunization in both exposed and control quail was not affected significantly. However, cell-mediated immune potential, measured by the reaction to intradermal injection of phytohemagglutinin-P in the wing web, was reduced in the exposed females, but not in the exposed males. Additionally, total leukocyte numbers and absolute circulating numbers of lymphocytes, monocytes, and heterophils were increased significantly only in the exposed females. These data show that exposure of Japanese quail during embryogenesis reduced cell-mediated immune potential and induced a general leukocytosis in females.

**

Study Type: Immunology and Hematology; IN VIVO; JAPANESE QUAIL
Effect Type: Alterations of humoral and cell-mediated immune potential in adult quail from RFR exposure of the embryos
Frequency: 2.45 GHz
Modulation: CW
Power Density: 5 mW/sq cm
SAR: 4.03 W/kg

EXPOSURE CONDITIONS: 6x5 arrays of eggs were exposed to far-field RFR in an anechoic chamber at 35.5 deg C and 60% relative humidity. Egg temperatures were 37.5 to 38.0 deg C. Each array was exposed 24 hr/day for the first 12 days of development. Arrays were automatically turned 90 deg every 2 hr. Control eggs were sham-exposed at 38.0 deg C but otherwise treated similarly.

OTHER INFORMATION: Following the 12-day RFR- or sham-exposure period, the eggs were transferred to an egg incubator. Upon hatching, the chicks were initially housed in heated metal cages for 1 week at 35 deg C and 2 weeks at 30 deg C, after which they were transferred to unheated cages at 25 deg C ambient temperature. When 6 weeks old, RFR-exposed males were paired with RFR-exposed females in mating cages, and the sham-exposed quail were similarly paired.

Humoral responses were ascertained in experiments 1 and 2, in which 22-week-old quail were immunized with chukar (partridge) red blood cells (CrRBC). The text states that blood samples were taken on days 0, 4,

and 7 after immunization and assayed for total anti-CrRBC hemagglutinins (for all 3 days) and for total and differential leukocytes (for days 4 and 7), but is ambiguous regarding day 0. Apparently the blood samples on day 0 were taken prior to injection with CrRBC, but the results (Table 1) were labeled as post-CrRBC. In any case, the results for day 0 indicate that the hemagglutinin levels for the RFR-exposed quail of both sexes were higher than for the corresponding sham-exposed quail; note that the differences for both sexes were labeled as significant ($p<0.05$), but by analysis of variance, only the difference for the females was significant. Also, neither the difference between the RFR-exposed males and females nor between the sham-exposed males and females was significant. Table 1 also shows that none of the differences by treatment or sex for day 4 or 7 was significant.

The anti-CrRBC anti-sera obtained in these experiments were also assayed for relative levels of IgM and IgG. The results (Table 2) show that for day 0, the levels of IgM for the RFR-exposed quail of both sexes were significantly higher than for the corresponding sham-exposed quail, with no significant differences between the sexes. Table 2 also shows no significant differences by treatment or sex for day 4 or 7. Regarding the IgG levels (Table 3), a significant decrease was found on day 0 for the RFR-exposed males only, but the difference between the RFR-exposed males and females was not significant. There were no significant differences between RFR- and sham-exposed males or females on day 4 or 7, but Table 3 shows that on day 7, the level of IgG for the control females was significantly higher than for the control males.

Regarding the elevated levels of IgM in the RFR-exposed quail on day 0 (prior to immunization), the investigators speculated that perhaps the quail had been exposed inadvertently to an antigen that evoked antibodies cross-reactive with CrRBC. This hypothesis is supported by the observation that the nonspecific hemagglutinin levels in these quail were also higher than for the controls. However, neither overt pathogenicity nor increase in mortality or morbidity was observed. Based on the negative findings with CrRBC for days 4 and 7, the investigators concluded that RFR exposure of quail embryos does not alter the humoral immune potential of the adult birds.

The total leukocyte numbers determined on days 0 and 7 (Table 5) indicate no significant differences between RFR-exposed and control males for either day. By contrast, the mean values for the RFR-exposed females were higher than for the corresponding control females. (The differences for both days were labeled significant, but by analysis of variance, the difference for day 0 would not be significant.) Mean numbers of lymphocytes, monocytes, heterophils, eosinophils, and basophils on day 0 and 7 are given in Table 6 without the standard errors of the means. The results indicate that the RFR-exposed females had more circulating lymphocytes and heterophils than the control females on both days, while the monocyte levels were higher only on day 7. RFR-exposed males had values comparable to those for control males on both days. The investigators noted that RFR exposure of quail embryos did not alter leukocyte numbers in the neonatal birds (McRee et

al., 1975), but they indicated that the hematologic system of the neonate quail is quite different from that of the adult bird.

Cell-mediated immune potential was evaluated in experiments 3 and 4 with 22-week-old quail that were RFR- or sham-exposed in the egg. The T-cell mitogen phytohemagglutinin (PHA-P) was injected in one wing web and saline in the other wing web of each quail. Skin thicknesses were measured before and 18 hr after injection (time of maximum responsiveness), and the web index, defined as the ratio of post-injection to pre-injection thickness, was calculated for each wing. The results for PHA-P (Table 4) indicate that the mean web index for the RFR-exposed females was significantly smaller than for the sham-exposed females, but the difference between the RFR- and sham-exposed males was not significant. Also, significant effects attributable to saline injection were not found in either sex. The investigators were unable to offer an explanation for this sex-dependent reduction of cell-mediated immune function, but suggested that the increase in circulating leukocytes in the RFR-exposed females, discussed above, may have been a compensatory response to this effect.

CRITIQUE: The description by the investigators of the statistical treatment of the data was brief and somewhat obscure. Presumably experiment 2 was a replicate of experiment 1, and similarly for experiments 3 and 4; the investigators found that they could pool the results of each pair of replicate experiments.

In the absence of results for day 0, the nonsignificant differences in hemagglutinin levels for days 4 and 7 (post-immunization) would indicate that the RFR exposure of the eggs had not altered the humoral immune potential of the quail. However, the results for day 0 (pre-immunization) show that the humoral levels of all four groups (RFR- and sham-exposed males and females) were significantly lower than the levels on days 4 and 7, but that the day-0 levels of the RFR-exposed male and female quail were both higher than their respective controls. These results would indicate that the RFR exposure did have a stimulative effect on the humoral immune potential, but that the effect was weak relative to that produced by the CrRBC. It should be noted, however, that in a previous investigation by this group (Hamrick et al., 1977), in which quail eggs were exposed similarly, no significant differences in hemagglutinin levels between RFR- and sham-exposed 5-week-old quail of either sex were found prior to immunization. (The results of this investigation also indicated that 4 days after immunization with sheep erythrocytes, the levels were significantly higher than before immunization, and that there were no significant differences in level between RFR- and sham-exposed quail of either sex, in consonance with the results of the later investigation.)

The increases of IgM level for RFR-exposed males and females on day 0 was characterized by the investigators as an enigma, and they speculated that perhaps the quail had been exposed inadvertently to an antigen that evoked antibodies cross-reactive with CrRBC. It should be noted that the variations of the IgM levels on days 4 and 7 as well as on day 0

were qualitatively similar to the variations of the hemagglutinin levels, so the latter may have a common etiology with the former. By contrast, the behavior of the IgG levels was different in that on day 0, the RFR-exposed males yielded a significantly lower level than the control males and that the difference for the females was not significant. On the other hand, on day 7, the IgG level for the control females was significantly higher than for the control males, a non-RFR effect. Cohabitation as mated pairs after age 6 weeks may have influenced the results.

Regarding total leukocyte counts, evidently the only significant difference between RFR- and sham-exposed quail was for the females on day 7 (a higher mean count for the former relative to the latter). However, the count for the RFR-exposed females was also significantly higher than for their RFR-exposed mates. These females exhibited higher differential counts of lymphocytes and heterophils on days 0 and 7, and higher monocyte counts on day 7 than the respective female controls. The monocyte results are at variance with the lower monocyte counts found by McRee and Hamrick (1977) in neonate quail exposed to RFR in the egg.

In experiments 3 and 4 (pooled data), the mean web index 18 hr after injection with PHA-P was significantly smaller for the RFR-exposed females than for the control females and the RFR-exposed males.

The apparently gender-related effects of this investigation are not understood and may have involved factors other than RFR exposure. In general, the results of this investigation can be characterized as equivocal.

REFERENCES:

Hamrick, P.E., D.I. McRee, P. Thaxton, and C.R. Parkhurst
HUMORAL IMMUNITY OF JAPANESE QUAIL SUBJECTED TO MICROWAVE RADIATION DURING EMBRYOGENY
Health Phys., Vol. 33, pp. 23-33 (1977)

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)

McRee, D.I., P.E. Hamrick, J. Zinkl, P. Thaxton, and C.R. Parkhurst
SOME EFFECTS OF EXPOSURE OF THE JAPANESE QUAIL EMBRYO TO 2.45-GHZ MICROWAVE RADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 377-390 (1975)

***

GALVIN
MCREE
HALL
THAXTON
PARKHURST

/

ANTIBODY
ANTIGEN
CW
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MITOGEN
QUAIL
RFR

//

1981
2450
1
5
4.03

///

100
Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b)

*

AUTHOR ABSTRACT: In order to assess the biological effects of long-term microwave radiation, special exposure systems were developed and used to expose four rabbits to 10-mW/sq cm microwave radiation (maximum 17 W/kg SAR) for 23 h per day for 180 days. Comparisons with four sham-exposed rabbits revealed no significant effects in terms of eyes, body mass, urinary output, rectal temperature, hematocrit, hemoglobin, white cell count, and basic blood-coagulation studies. After the experiment, the animals were sent to the National Institute of Environmental Health Sciences for additional analyses which revealed biochemical effects as reported in a companion paper in this issue.

**

Study Type: Ocular Effects, Immunology and Hematology;
IN VIVO; RABBIT
Effect Type: RFR-induced eye damage and alterations of hematology
Frequency: 2.45 GHz
Modulation: CW
Power Density: 10 mW/sq cm
SAR: 17 W/kg (max) in the head (measured); 1.5 W/kg whole body (calculated)

EXPOSURE CONDITIONS: Four rabbits housed in acrylic cages were concurrently exposed dorsally in individual anechoic chambers to 2.45-GHz CW RFR 23 hr/day for 180 days in the far field of a horn in each chamber. The electric vector was parallel to the long axis of the rabbit. Four other rabbits were sham-exposed in similar chambers concurrently with the RFR-exposed rabbits. The 8 chambers were maintained at 24 deg C by a common air conditioner.

OTHER INFORMATION: Dorsal exposure, selected for compactness in multiple-chamber design, was rather uncommon in prior investigations. Therefore, in preliminary dosimetric experiments, rabbits were exposed laterally and dorsally to determine the respective power densities needed to produce the same mean SAR in the eye. The exposures were for 15 seconds at 525 mW/sq cm measured at eye location, and a thermocouple was used to measure SAR as a function of depth in the eye. Greater variation of SAR was obtained for dorsal exposure, but the spatial-average SARs for the eye were comparable: 0.679 and 0.481 W/kg per mW/sq cm for dorsal and lateral exposure, respectively.

The effective power-density patterns in the acrylic-cage region of each exposure chamber were mapped along the horn axis and in the E- and

H-planes of the horn, with and without the empty cage present. The data were used to ascertain the input power necessary to obtain 10 mW/sq cm at the location of the rabbit's head (with the rabbit absent). With this input power (32 W), the power density at the central location of the animal was about 7 mW/sq cm.

Lines of constant SARs were obtained by the use of thermography on rabbit carcasses. The results indicated that this input power would produce a peak SAR of 17 W/kg in the head when the animal is in the normal resting position in the cage. By calculation, the whole-body SAR for a prolate-spheroidal model of a rabbit exposed to 2.45-GHz RFR at 10 mW/sq cm is about 1.5 W/kg.

Periodic eye examinations with a slit-lamp microscope were made during the exposure period. Aside from normal aging changes in the lenses of the 8 animals, no differences in the eyes of the RFR- and sham-exposed groups were seen.

Also monitored periodically during the exposure period were: body mass, urinary output, rectal temperature, hematocrit, hemoglobin, total and differential leukocyte counts, platelet count, and basic blood-coagulation indices. Statistical treatment of the results showed apparently significant decreases in percentage of eosinophils in the RFR-exposed group but no other significant differences between groups for the remaining parameters. However, the eosinophil percentage varies widely among animals.

Additional tests were performed subsequently on the same animals at the National Institute of Environmental Health Sciences. The results were presented in a companion paper by McRee et al. (1980).

CRITIQUE: Although most of the features of the multiple-chamber exposure system were described, including the virtually RFR-transparent water-supply and urine-collection devices, the method for collecting and/or removing feces from the chambers was not discussed.

The finding of no ocular damage from 6 months of almost continuous exposure (23 hr/day) at 10 mW/sq cm is not only consistent with the existence of an RFR-cataractogenesis threshold exceeding 100 mW/sq cm for relatively shorter exposure durations (Williams et al., 1955; Guy et al., 1974; Carpenter, 1977), but also supports the conclusion that eye damage would not occur from indefinitely long exposure at 10 mW/sq cm or less.

Examination of the hematological results (Table 1) shows that several other indices besides the eosinophil percentage varied widely among the animals, as evidenced by the large differences in their standard deviations per se. (Such large differences often indicate that unknown factors were influencing the results.) For example, the initial (pre-exposure) percentages of lymphocytes for the RFR- and sham-exposed groups were 45.5 +/- 15.4 and 60.3 +/- 1.5, respectively, a 10:1 ratio of standard deviations for roughly comparable means.

Treatment of the data by, say, analysis of variance would show other statistically significant ($p<0.05$) differences between the groups. For example, the monocyte percentage was lower following 4.5 months of RFR exposure ($F=7.20$, $df=1/6$). Note, however, that the differences for shorter (0, 1.5, 3 months) and longer (6 months) exposures were not significant. In addition, there would be significant differences within each group during the course of exposure, e.g., between the initial- and 1.5-month basophil percentages for the RFR group ($F=10.32$). Therefore, the investigators were probably correct in not ascribing RFR-related biological significance to such differences.

REFERENCES:

Carpenter, R.L.
MICROWAVE RADIATION
In D.H.K. Lee (ed.), HANDBOOK OF PHYSIOLOGY, American Physiological Society, Bethesda, Maryland, pp. 111-125 (1977)

Guy, A.W., J.C. Lin, P.O. Kramar, and A.F. Emery
QUANTITATION OF MICROWAVE RADIATION EFFECTS ON THE EYES OF RABBITS AT 2,450 MHZ AND 918 MHZ
University of Washington Scientific Report No. 2, Seattle, WA (1974)

McRee, D.I., R. Faith, E.E. McConnell, and A.W. Guy
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: EVALUATION OF HEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 45-52 (1980)

Williams, D.B., J.P. Monahan, W.J. Nicholson, and J.J. Aldrich
BIOLOGICAL EFFECTS OF STUDIES ON MICROWAVE RADIATION: TIME AND POWER THRESHOLDS FOR THE PRODUCTION OF LENS OPACITIES BY 12.3-CM MICROWAVES
AMA Arch. Ophthalmol., Vol. 54, pp. 863-874 (1955)

***

GUY
KRAMAR
HARRIS
CHOU

/

CHRONIC
CW
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
OCULAR
PHYSIOLOGY
RABBIT
RECTAL
RFR
WEIGHT

//

1980
2450
1
10
1.5-17

///

101
Sulek, K., C. J. Schlagel, W. Wiktor-Jedrzejczak, H. S. Ho, W. M. Leach, A. Ahmed, and J. N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980)

*

AUTHOR ABSTRACT: A significant increase in the percentage of spleen cells bearing the receptor for the third component of complement (CR+) was induced in mice following a single exposure to 2450-MHz microwave radiation in an environmentally controlled waveguide facility (24 deg C, 50% relative humidity, 38 liters/min airflow). This increase was composed of surface immunoglobulin-positive, Thy-1-negative cells, and was observed by 3 days following exposure; it persisted for 5-6 days and returned to baseline levels by 9-10 days after exposure. No secondary increases were observed.

The threshold level of absorbed energy required to trigger the inductive events was determined using two experimental protocols: (a) varying the time of exposure to a constant forward power (0.6 W), or (b) maintaining a constant time of exposure while varying the forward power (0.1 to 0.78 W). It was determined that a minimum of a single 15-min exposure (0.6 W; 11.8 W/kg; 10.6 J/g) or a single 30-min exposure (0.3 W; 5.0 W/kg; 9.07 J/g) induced a significant increase on Day 3, which peaked on Day 6. Once this critical threshold level of absorbed energy (9.07-10.6 J/g) was attained, the induced response was maximal.

The effect of the absorption of multiple subthreshold quantities of microwave energy was cumulative, provided the exposures occurred within 1 hr of one another. When 24 hr elapsed between the exposures, the induced increase in CR+ cells was not observed, even though the total absorbed dose was at a level that would induce an increase if given in a single exposure. The induction of the increase in CR+ cells and its magnitude was independent of average dose rate in the range of 10-18 W/kg and weight of adult animals in the range of 18-25 g. The results indicate that the absorption of a critical threshold of microwave energy (approximately 9.07-10.6 J/g) is a prerequisite for the triggering of the inductive events which result in a significant increase in CR+ spleen cells.

**

Study Type: Immunology and Hematology; IN VIVO; MOUSE
Effect Type: Threshold for RFR-induced increases in spleen cells having complement receptors (CR+ cells)
Frequency: 2.45 GHz
Modulation: CW
Power Densities: Not given; 0.1 to 0.78 W forward power in waveguide
SAR: 2.7 to 16.1 W/kg

EXPOSURE CONDITIONS: Mice restrained in polystyrene holders were exposed individually at 0.6 W forward power (SAR of 11.8 W/kg) for 5 to 120 min or at 0.1 to 0.78 W (SAR of 2.7 to 16.1 W/kg) for 15 min in a waveguide system at 24 deg C, 50% relative humidity, and 38 ml/min air flow. Exposures were primarily with the mouse facing the source. Sham-exposed mice served as controls.

OTHER INFORMATION: The whole-body SAR (termed the "average absorbed dose rate" or ADR by the investigators) was the net power absorbed by each mouse divided by its weight just before exposure. Thus, at any fixed input power, the mean SAR varied from group to group. The absorbed dose was calculated by multiplying the SAR by the exposure duration.

In one set of experiments, groups of 6 mice of the CBA/J strain were sham-exposed or exposed at 0.6 W (mean SAR of 11.8 W/kg) for 30 min. At intervals following exposure, the spleens were removed and assayed for percentages of cells having surface immunoglobulin (sIg+) or receptors for: theta antigen (Thy-1.2+), spontaneous rosette formation with sheep red blood cells (SRBC rosettes), the Fc part of Ig (FcR+), or complement (CR+). The results for day 8 after exposure (Table I) showed significantly ($p < 0.05$) higher percentages of FcR+ and CR+ cells for the RFR-exposed than for the sham-exposed mice, and nonsignificant differences for the other assays. In addition, 97% of the CR+ cells were also Ig+ and none were Thy-1.2+, so most of the CR+ cells were B-lymphocytes. Assays for groups of 4 mice at 2-day intervals after exposure (Fig. 1) showed no significant difference in the percentage of CR+ cells on day 2; significantly higher percentages for the RFR-exposed mice on days 4, 6, and 8; and baseline percentages on days 10 through 18.

To determine the exposure-duration threshold for increasing the percentage of CR+ cells, groups of 6 mice were exposed at 0.6 W for 5 to 120 min, and their spleens were assayed for CR+ cells on day 3 or 6 after exposure. The results for day 3 (Table II) indicated increases of 1, 5, and 17% for RFR exposures of 5, 10, and 15 min, respectively, all of which were nonsignificant; increases ranging from 30 to 42%, all labeled significant ($p < 0.01$ or 0.001), were obtained for 20- to 120-min exposures. For day 6 (Table II), increases of 3% and 2% (not significant) were obtained for 5- and 10-min exposures, respectively, and increases ranging from 45% to 62%, all labeled significant ($p < 0.001$), were obtained for 15- to 120-min exposures. Thus, 15 min was taken as the exposure-duration threshold for a single exposure at a mean SAR of 11.8 W/kg. The corresponding absorbed dose was 10.6 J/g. For the longer exposures, the absorbed dose increased monotonically with exposure duration (but not linearly, because of the SAR variations among groups). However, the percentage increase of CR+ cells was not monotonic with either exposure duration or absorbed dose for either assay day.

Groups of mice were then exposed for 30 min at 0.1 to 0.78 W (SARs of 2.6 to 16.1 W/kg) and assayed for CR+ cells on day 3 or 6 after exposure. For both assay days (Table III), nonsignificant negative

increases (-1% and -2%) were found for 0.1 and 0.2 W. For day 3, significant ($p < 0.05$) increases ranging nonmonotonically from 24.4 to 33.7% were reported for 0.3 to 0.7 W, but the increase at 0.78 W was only 12% and nonsignificant. For the 0.3 W (30 min) threshold, the mean SAR was 5.0 W/kg and the absorbed dose was 9.07 J/g. For day 6, the increases for 0.3 to 0.78 W ranged nonmonotonically from 11.4 to 53.6% and were significant except for the value at 0.7 W (11.4%). For the 0.3 W threshold, the mean SAR and absorbed dose were 5.5 W/kg and 10.01 J/g, respectively. Taken together, the results indicated that triggering the events that led to significant percentage increases of CR+ cells required absorption of a minimum (threshold) energy in the range 9.07 to 10.6 J/g (for a single exposure).

Most exposures were made with the mouse facing the source (head-to-tail orientation). Exposures at suprathreshold absorbed doses in other orientations (tail-to-head, left-to-right, right-to-left) yielded small changes in absorbed dose, and all of the percentage increases of CR+ cells were significant (Table V).

Multiple exposures at 0.6 W for durations that each yielded a subthreshold value of absorbed dose were administered during successive hours in a single day. No significant percentage increases of CR+ cells were obtained for summed absorbed doses below the approximately 10 J/g threshold, whereas significant increases were seen for all summed doses exceeding the threshold except in one case (Table VI). Mice were also exposed once per day at 0.6 W for 5 min on successive days up to 5 days. The summed dose for 2 days was subthreshold whereas those for 3, 4, and 5 days exceeded the threshold (Table VII). Nevertheless, *no significant* changes in CR+ percentages were obtained for any of these cases.

Rectal temperatures were taken immediately before and after a single exposure at 0.1, 0.2, 0.6, or 0.78 W for 30 min, or at 0.6 W for 120 min. The largest temperature increase, 0.6 deg C, was obtained at 0.78 W and at 0.6 W for 120 min; the increase at 0.6 W for 30 min was only 0.1 deg C whereas the increase at 0.1 W (for 30 min) was 0.5 deg C (Table VIII). Rectal temperatures of mice sham-exposed for the same durations also showed increases of up to 0.4 deg C (for those treated for 120 min). On day 3 after such treatments, significant percentage increases in CR+ cells were found for 0.2 W (30 min), 0.6 W (30 and 120 min), but not for 0.78 or 0.1 W (30 min).

CRITIQUE: As in a previous paper from this group (Wiktor-Jedrzejczak et al., 1977), the statistical treatment of the data is unclear. First, use of the mean percentages, in Table I, of CR+ cells and the corresponding standard errors (SEs) for the RFR- and sham-exposed mice in the Student t-test yields $t = 3.25$. For 6 mice in each group ($f = 10$), this value is indeed indicative of a significant increase, but at a higher confidence level than stated ($p < 0.01$ rather than $p < 0.05$). However, a similar calculation for the FcR+ data yields $t = 1.65$, which corresponds to $p > 0.05$ (nonsignificance) rather than to $p < 0.05$ as stated. Second, the results presented in Tables II-VI are in the form of percentage increases of CR+ cells for the RFR-exposed mice relative

to the values for the sham-exposed controls rather than as means and SEs for both groups. In this context, it should be noted that the SEs in Table VII are severalfold larger than the CR+ SEs in Table I. Third, although the investigators indicated that each RFR- and sham-exposed group comprised 6 mice, some of the results presented (e.g., Fig. 1) were for 4 mice/group, and it is not clear whether only 4 mice/group were treated or that the data for 2 mice/group were not included. Last, the criterion for positive rosette was stated as 3 or more adherent erythrocytes for Table I, and as 5 or more in Fig. 1.

Despite the points above, the results support the conclusion that single exposures to RFR at absorbed doses exceeding a threshold of about 10 J/kg of body weight can increase the percentage of CR+ B-lymphocytes in the mouse spleen. Similar results were obtained with 3 or more doses, each about 1/3 the threshold, if the doses were administered hourly. By contrast, administering such subthreshold doses at 24-hr intervals yielded negative results, i.e., the doses were not cumulative in effect. As indicated by the investigators, this effect appears to be an "all-or-none" phenomenon not having a discernible dose-response relationship, and they speculate that a fixed number of lymphocytes are susceptible to, and are recruited by, the RFR above the threshold.

There was also no discernible relationship among the CR+ cell increases, the SARs, and the small rectal-temperature increases of the RFR-exposed mice. Moreover, the sham-exposed mice also exhibited small temperature increases. The latter point may be an indication that the mice were stressed, possibly from restraint during treatment and/or from handling before and after treatment.

REFERENCES:

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W. M. Leach, and K. W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977)

***

SULEK
SCHLAGEL
WIKTOR-JEDRZEJCZAK
HO
LEACH
AHMED
WOODY

/

ANTIBODY
ANTIGEN
COMPLEMENT
CW
IMMUNOLOGY
IN-VIVO
LYMPHOCYTE
MOUSE
RECTAL
RFR
STRESS
THRESHOLD

//

1980
2450
1
0
2.7-16.1

///

102
Liburdy, R. P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)

*

AUTHOR ABSTRACT: In vivo lymphocyte circulation was significantly altered in mice exposed to whole-body radiofrequency radiation (RFR). In vivo lymphocyte circulation was followed by quantitating activity of sodium chromate-51-labeled lymphocytes in the lung, spleen, liver, and bone marrow of animals at different times after iv spleen lymphocyte injection. Immediately after cell injection, animals were exposed to 2.6-GHz RFR (CW) at 25 or 5 mW/sq cm (3.8 W/kg) for 1 hr. At 1, 4, and 24 hr after lymphocyte injection target organs were removed, weighed, and counted. Sham RFR, warm-air, and steroid-treated groups were included as controls.

Hyperthermic RFR exposure (25 mW/sq cm; 2.0 deg C increase in core temperature) led to a 37% reduction in lymphocytes leaving the lung to migrate into the spleen. In addition, a threefold increase in spleen lymphocytes entering the bone marrow occurred. Significantly, this pattern was also observed in the steroid-treated group; nonthermogenic RFR exposure (5 mW/sq cm) and warm-air exposure did not lead to altered lymphocyte traffic. These results support the idea that steroid release associated with thermal stress and the process of thermoregulation is a significant operant factor responsible for RFR effects on the immune system.

**

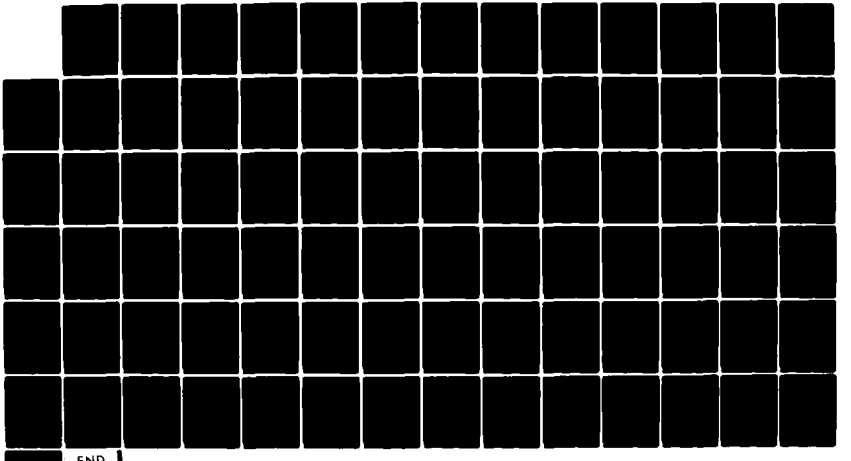
Study Type: Immunology and Hematology, Endocrinology; IN VIVO; MOUSE
Effect Type: Alterations of circulating lymphocyte traffic by thermogenic RFR and glucocorticoid injection
Frequency: 2.6 GHz
Modulation: CW
Power Densities: 25 or 5 mW/sq cm
SAR: 19 or 3.8 W/kg

EXPOSURE CONDITIONS: Mice were exposed in an anechoic chamber to far-field, 2.6-GHz RFR. It is not clear whether the longest body axis was parallel to the E-vector as stated in the text or to the propagation direction ("KEH" orientation) as stated in Ref. 6 of the paper. RFR exposures at 25 mW/sq cm (SAR 19 W/kg) and 5 mW/sq cm (3.8 W/kg) were defined as "thermogenic" and "nonthermogenic," respectively. Other groups of mice were sham-exposed as controls or heated in a warm dry-air oven at 63 deg C. All such treatments were for 1 hr.

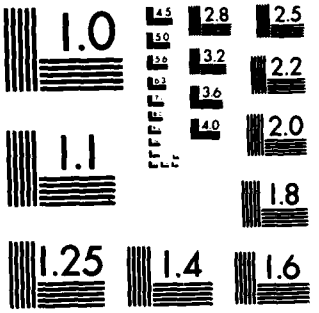
OTHER INFORMATION: Rectal temperature was monitored continuously with an RFR-transparent thermometer during the 1-hr exposure to RFR or warm air. Exposure to thermogenic RFR (SAR 19 W/kg) produced a 2 deg C rise in

AD-A140 023 USAFSAM (USAF SCHOOL OF AEROSPACE MEDICINE) REVIEW AND ANALYSIS OF RADIOF..(U) SRI INTERNATIONAL MENLO PARK CA L N HEYNICK ET AL. MAR 84 USAFSAM-TR-84-6

UNCLASSIFIED F33615-82-C-0610 F/G 6/18 NL



END
DATE FILMED
6-84
DTIC



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

deg C within 15 min, which was maintained by the mice for the remainder of the period by thermoregulation. The warm-air treatment (at 63 deg C) caused a rise to the same plateau, but in 30 min. The author emphasized this difference in thermoregulation and noted that steroid output in RFR-heated mice is threefold higher than in mice heated in warm air to the same plateau core temperature (Liburdy, 1979). After cessation of treatment, the return rate to baseline (37 deg C) was the same for both treatments. Nonthermogenic RFR (5 W/kg) yielded no significant rectal temperature increase. Mice injected with the glucocorticoid methylprednisolone sodium succinate served as a steroid treatment group.

Splenic lymphocytes radiolabeled with Cr-51 were injected into the lateral tail vein of syngeneic mice just prior to sham-, RFR (either level)-, or warm-air exposure or steroid injection. At 1, 6, or 24 hr after lymphocyte injection, the lung, liver, spleen, and long bones of the rear legs were removed and assayed for radioactivity by scintillation counting. Relative radioactivity was calculated as counts per min per organ weight and normalized to the total activity recovered in the four tissues assayed. Total activity recovered exceeded 90% of the activity injected.

Lung assays at 1 hr after injection yielded relative radioactivities of about 80 to 85%, with no statistically significant differences among the five treatment modalities, indicating that most of the lymphocytes flowed into the lung irrespective of the type of treatment. At 6 hr, the relative radioactivities for the sham-, warm-air, and nonthermogenic-RFR treatments were about 55%, indicating significant lymphocyte egress from the lung. However, the egress was smaller for the thermogenic-RFR and steroid treatments, yielding activities of about 71% and 78%, respectively. At 24 hr, the activity for the sham-, warm-air, and nonthermogenic-RFR treatments were about 40%, and the values for the steroid and thermogenic-RFR treatments were about 50% and 64%.

For the spleen, the activities were about 12% at 1 hr for all five treatments. The values for the sham-, warm-air, and nonthermogenic-RFR treatments rose to about 35% at 6 hr and to about 40% at 24 hr, indicating significant lymphocyte influx into the spleen concurrent with the rapid egress from the lung for these three treatments. The splenic activities for the steroid and thermogenic-RFR treatments rose to only about 20% at 6 hr and only slightly higher at 24 hr, again concurrently with the slower lymphocyte egress from the lung for these two treatments.

Activities in the liver were about 6% at 1 hr, between 7 and 8% at 6 hr, and 9 to 10% at 24 hr, with no large differences among the five treatments.

In the bone marrow, there were significant differences at all three assay times between the values for the sham , warm-air, and nonthermogenic-RFR groups, as compared with the values for the steroid and thermogenic-RFR groups. Less than 1% activity was seen for the first three groups at 1 hr, with only slight increases at 6 and 24 hr to

about 1%. By contrast, the activities for the thermogenic-RFR and steroid groups were respectively about 1.5% and 2.2% at 1 hr, 2.7% and 2.9% at 6 hr, and 2.9% and 3.1% at 24 hr. Although these activities were small relative to those for the other tissues, they indicated a threefold higher lymphocyte flow into the bone marrow for the latter two treatments.

In summary, at 1 hr after injection, about 80% of the radiolabeled splenic lymphocytes were in the lung, 12% in the spleen, 5% in the liver, and the remainder in the bone marrow irrespective of treatment. For the sham-, warm-air, and nonthermogenic-RFR groups at 6 hr, about 30% of the lymphocytes migrated from the lung to the spleen. By contrast, for the thermogenic-RFR group at 6 hr, lymphocyte flow from the lung to the spleen was only about 10%, and there was a threefold increase in the small percentage of lymphocytes in the bone marrow. The results for the steroid group were qualitatively similar to those for the thermogenic-RFR group.

CRITIQUE: The flow of most of the injected radiolabeled splenic lymphocytes to the lung during the first hour irrespective of treatment modality was denoted by the investigator as "normal." The relative changes from the initially high levels of lymphocytes in the lung due to the different treatment modalities are consonant with the findings in previous studies with mice by this investigator (Liburdy, 1977, 1979) and of Lotz and Michaelson (1978) with rats, which support the hypothesis that the heat generated by thermogenic RFR triggers the ultimate release of adrenal steroids that alter the distribution of lymphocytes.

As noted by the investigator, steroid output in mice heated with thermogenic RFR is threefold higher than in mice heated with warm air to the same plateau core temperature (Liburdy, 1979). Presumably this observation accounted for the absence of lymphocyte circulation changes from warm-air treatment, i.e., the nonsignificant differences in results for this treatment and sham-exposure.

Another important result is that nonthermogenic RFR as defined herein (2.6 GHz at an SAR of 3.8 W/kg for 1 hr) yielded essentially the same results as for sham-exposure.

REFERENCES:

Liburdy, R. P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977)

Liburdy, R. P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

Lotz, W. G. and S. M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiology, Vol. 44, No. 3, pp. 438-445 (1978)

***

LIBURDY

/

CORTICOSTEROID
CW
ENDOCRINOLOGY
HYPERTHERMIA
IMMUNOLOGIC
IN-VIVO
LYMPHOCYTE
MOUSE
RECTAL
RFR
THERMOREGULATION
TRACER

//

1980
2600
1
5-25
3.8-19

///

103
Liburdy, R. P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHYOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

*

AUTHOR ABSTRACT: Acute transient lymphopenia in the mouse was induced by whole-body exposure to radiofrequency radiation (RFR) (26 MHz, 2 deg C increase in core temperature over 15 min). Mice experiencing RFR-induced lymphopenia showed a relative increase in splenic T- and B-lymphocytes; these elevated levels were further pronounced by three RFR exposures delivered at 3-hr intervals. Multiple RFR exposures also led to a significant decrease in thymic weight and thymic and splenic cell density and, moreover, to suppressed cell-mediated immune function as measured in vivo by local delayed-type hypersensitivity. Only splenic B-lymphocyte levels were elevated with no change in delayed hypersensitivity in warm air-exposed mice (2 deg C increase in core temperature over 15 min).

Plasma corticoid levels immediately after RFR treatment were severalfold higher than those in mice given warm air or sham exposure. Notably, administration of methyl prednisolone sodium succinate to control animals led to lymphopenia, increased splenic T- and B-lymphocyte frequency, and thymic involution that was observed in RFR exposed animals. These results indicate that RFR hyperthermia can induce significant alterations in lymphocyte distribution and function and that RFR impact on the immune apparatus appears to be mediated at the cellular level indirectly through steroid-associated actions.

**

Study Type: Immunology and Hematology, Endocrinology; IN VIVO; MOUSE
Effect Type: RFR-induced lymphopenia and neutrophilia and increases in splenic T- and B-lymphocytes
Frequency: 26 MHz; 5 MHz
Modulation: CW
Power Densities: (1) 800 mW/sq cm at 26 MHz; (2) 50 mW/sq cm at 16 MHz or 800 mW/sq cm at 5 MHz
SAR: (1) 5.6 W/kg; (2) 0.36 W/kg

EXPOSURE CONDITIONS: Immobilized mice were sham-exposed or exposed to RFR with long axis parallel to the E-vector in a TEM cell at 25 deg C and 45% humidity. Acute "thermogenic" RFR exposure was one 15-min session to 26 MHz at 800 mW/sq cm (SAR 5.6 W/kg), which yielded a core temperature rise of 2-3 deg C. Acute "nonthermogenic" RFR exposure was one 15-min session to either 26 MHz at 50 mW/sq cm (0.36 W/kg) or 5 MHz at 800 mW/sq cm (same SAR). Chronic RFR exposure consisted of 15-min sessions per day at 0900 and 1500 for 10 days to thermogenic RFR (20 sessions total). Other mice were either heated in a dry-air oven at 63

deg C or immersed in a water bath at 41 deg C for 15 min, to yield 2-3 deg C core temperature rises.

OTHER INFORMATION: Thermogenic RFR treatment yielded a linear increase in core temperature from about 37 to 40 deg C in 15 min. The water-immersion treatment produced an increase to 39 deg C in the first 5 min, followed by a slow rise to 40 deg C, whereas the curve for the hot-air treatment was closer to that for the RFR. Consequently, results for water immersion were not given.

Measurements of peripheral-blood lymphocyte and neutrophil populations were made just before and after treatment and subsequently at 1-hr intervals. The results for acute thermogenic RFR showed significant lymphopenia and neutrophilia that reached maxima at 3 hr posttreatment. The lymphopenia persisted for 12 hr and the neutrophilia for about 24 hr. The corresponding curves for the acute warm-air treatment showed small but presumably nonsignificant changes. No significant alterations of the lymphocyte and neutrophil populations were obtained for sham-exposure or exposure to either form of acute nonthermogenic RFR. The maxima of lymphopenia and neutrophilia obtained 3 hr postexposure could be sustained for more than 15 hr by two additional acute thermogenic-RFR exposures at 3-hr intervals. A single injection of the glucocorticosteroid methylprednisolone sodium succinate produced a qualitatively similar time course of sustained peripheral-blood lymphopenia and neutrophilia, but also a diminution of total leukocyte population.

The degree of stress due to RFR heating was determined by measuring plasma corticoid levels, and weights and cell densities of the thymus and spleen after acute or chronic treatments. Following either acute or chronic thermogenic-RFR exposure, the plasma corticoid levels were threefold higher than for sham-exposed controls or for mice treated acutely or chronically with warm air, with nonsignificant differences among the latter three groups. Thymus weights and cell densities for the group chronically exposed to the RFR were significantly lower than for the acute-RFR, warm-air, and control groups. There were no significant differences in splenic weight among the four groups, but the splenic cell density was significantly lower for the chronic-RFR group. Injection of the glucocorticoid steroid also produced significantly lower values of thymus and spleen cell density and thymus weight.

At maximum lymphopenia (3 hr after acute or chronic exposure to RFR), percentages of T- and B-lymphocytes in the spleen were determined. Acute RFR exposure yielded marked enrichment of both T- and B-lymphocytes in the spleen, with further enhancement by chronic RFR exposure. Assays 6 hr after steroid injection also yielded increases of both classes of lymphocytes. By contrast, acute and chronic warm-air treatments yielded increases of B-lymphocytes only.

Last, delayed-type hypersensitivity (DTH) was ascertained by sensitizing mice with sheep red blood cells (SRBC) by injection, challenging the mice 4-5 days later by SRBC injection into the right-rear footpad (while

injecting saline into the left-rear footpad), and measuring the swelling of the right-rear footpad relative to the left-rear one 24 hr after challenge. The mice were chronically exposed to thermogenic RFR or warm air from 5 days prior to sensitization to the day of challenge. The warm-air treatment yielded DTH results comparable to those for sham-exposed controls, but chronic RFR exposure markedly depressed the DTH response.

Because steroid injection yielded results qualitatively similar to those for thermogenic RFR, the investigator concluded that a causal relationship exists between RFR hyperthermia, steroid release, and alterations of lymphocyte distribution and function. The suggested mechanisms involves RFR stimulation of the hypophyseal-hypothalamic-adrenal axis through heating, which triggers the release of adrenal steroids that act directly on the lymphocytes to alter their distribution and function.

CRITIQUE: In a previous paper (Liburdy, 1977), this investigator presented experimental evidence to support the hypothesis that the effects of RFR on the immune system are primarily due to heat-stimulated release of glucocorticoids that alter lymphocyte circulation. The results of the later investigation with thermogenic and nonthermogenic RFR and with steroid injection comprise additional experimental evidence to support this hypothesis. The investigator also cautions that further experiments would be necessary to ascertain whether other stress-associated products, such as those from the adrenal medulla, are contributory factors.

The investigator emphasized that relative enrichment of T- and B-lymphocytes in the spleen was seen at the time when peripheral-blood lymphopenia was at its maximum, an indication that thermogenic RFR altered the distribution of lymphocytes rather than their total populations. In a subsequent investigation (Liburdy, 1980), the results showed that the time course of lymphocyte populations in the lung, spleen, and bone marrow were indeed altered by thermogenic RFR. However, the RFR appeared to reduce the flow of lymphocytes from the lung to the spleen. Specifically, such migration was significantly slower than for sham-exposed mice. Nevertheless, the observation that the T- and B-lymphocyte total subpopulations were not significantly altered by thermogenic RFR is consonant with the results of Wiktor-Jedrzejczak et al. (1980), which showed that increases in B-lymphocytes (CR+) induced by RFR were not due to elevated cell proliferation.

The panleukocytosis observed for sham and warm-air exposed mice from Liburdy (1977) was not observed in Liburdy (1979). This was not discussed by Liburdy, nor are the reasons for the difference readily apparent.

REFERENCES:
Liburdy, R. P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977)

Liburdy, R. P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W. M. Leach, and K. W. Sell
EFFECT OF MICROWAVES (2450-MHZ) ON THE IMMUNE SYSTEM IN MICE: STUDIES OF NUCLEIC ACID AND PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 1, No. 2, pp. 161-170 (1980)

***

LIBURDY

/

ANTIBODY
ANTIGEN
CORTICOSTEROID
CW
ENDOCRINOLOGY
HYPERTHERMIA
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MOUSE
RECTAL
RFR
STRESS
WEIGHT

//

1979
5-26
1
50-800
0.36-5.6

///

104
Szmigielski, S., W. Roszkowski, M. Kobus, and J. Jeljaszewicz
MODIFICATION OF EXPERIMENTAL ACUTE STAPHYLOCOCCAL INFECTIONS BY LONG-TERM EXPOSITION TO NON-THERMAL MICROWAVES OR WHOLE BODY MICROWAVE HYPERTHERMIA
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 127-132 (June-July 1980)

*

AUTHOR ABSTRACT: Environmental factors, including non-ionizing radiation may exert either a specific or toxic effect on cells and organs or lead to non-specific stress reaction and/or adaptation syndrome. This may in turn lower the natural antibacterial and antineoplastic resistance. In the review based on the own experiments performed in 1974-1979 the increased sensitivity of mice and rabbits to acute staphylococcal infections caused by long-term irradiation in non-thermal microwave fields will be discussed with special emphasis on reactivity of granulopoiesis. Whole-body microwave hyperthermia results in temporary suppression of cell-mediated immune reactions, while after irradiation in non-thermal microwave fields the inhibited reaction of granulopoiesis was found. Both these phenomena resulted in increased mortality from acute staphylococcal infections. The possible role of the non-specific stress reaction occurring in animals exposed to non-thermal microwave fields will be discussed.

**

Study Type: Immunology and Hematology, Medical Applications;
IN VIVO; MOUSE, RABBIT
Effect Type: Effects of low- and hyperthermic levels of RFR on survivability, granulopoiesis, phagocytosis, and other functions of the immune system in animals infected postexposure with Staphylococcus aureus
Frequency: 2.45 GHz
Modulation: CW or Pulsed: 1- or 2-microsecond pulses, peak power density or duty cycle not stated
Power Densities: 5 or 15 mW/sq cm Av ("nonthermal"); 30-40 mW/sq cm ("hyperthermic")
SAR: Nonthermal: 2-3 or 6-9 W/kg; hyperthermic: not stated

EXPOSURE CONDITIONS: Mice or rabbits were exposed to far-field 2.45-GHz RFR in a temperature- and humidity-controlled anechoic chamber for 2 hr/day at 5 or 15 mW/sq cm for 6 or 12 weeks before infection with Staphylococcus aureus, or for 2 hr/day at 30-40 mW/sq cm for 4, 7, 10, or 14 days before infection.

OTHER INFORMATION: In the "nonthermal" aspects of this investigation, mice and rabbits were exposed at 5 or 15 mW/sq cm for 6 or 12 weeks, which produced no detectable rectal-temperature increases. After completion of exposure, the animals were injected with viable Staphylococcus aureus.

In the rabbits, injection resulted in increased body temperature and leukocytosis lasting 5-7 days, with spontaneous recovery after 10-14 days and no deaths. Tests for blood granulocytosis, release of bone-marrow-reserve granulocytes after injection with purified staphylococcal alpha-toxin, serum lysozyme activity, and percentage of positive granulocytes observed with nitroblue tetrazolium (NBT) dye were performed on days 4, 6, 10, and 14 after infection. From Fig. 3, granulocytosis, peaking on day 6, and serum lysozyme activity, peaking on day 4, were evident in the control rabbits and in the rabbits exposed at 10 mW/sq cm (a level not mentioned elsewhere) for 6 weeks, but were virtually absent in the rabbits exposed for 12 weeks. Release of bone-marrow-reserve granulocytes, peaking on day 6, was higher for controls than for the animals exposed for 6 weeks, and was absent for those exposed for 12 weeks. The NBT test showed approximately the same peak for all three groups on day 4; during the remainder of the 14-day test period, the percentage of NBT-positive granulocytes persisted at peak level for the 12-week group, diminished gradually for the 6-week group, and decreased more abruptly for the controls.

In the mice, the dose of S. aureus given after RFR exposure was selected to be lethal for 40% of control mice in 3 days. (The text states 60% lethality, but the data presented in Fig. 4 shows a 60% survival rate for controls.) Groups of 20 mice each were exposed at 5 or 15 mW/sq cm for 6 or 12 weeks. Of the mice exposed at 5 mW/sq cm for 6 weeks, 4 died on day 1 and none afterward, for a 3-day survival rate of 80%. For the control group, 5 died on day 1, 2 more on day 2, and 1 more on day 3, yielding the 60% 3-day survival rate. Of the mice exposed at 5 mW/sq cm for 12 weeks, 6 died on day 1, 5 more on day 2, and none on day 3, for a 45% survival rate. The differences among these three groups were denoted as nonsignificant. For the groups exposed at 15 mW/sq cm for 6 or 12 weeks, the daily survival rates were successively lower, culminating in 3-day rates of 25% (5 mice) and 5% (1 mouse), respectively.

Phagocytosis of S. aureus by isolated peritoneal macrophages was lower in mice exposed at 15 mW/sq cm for 12 weeks than in controls, and was higher in mice exposed at 5 mW/sq cm for 6 weeks. The differences for the other two RFR-exposed groups were not significant. There were no significant differences in delayed hypersensitivity to oxazolone among the four RFR-exposed groups and the controls.

In the other part of the investigation, whole-body hyperthermia (rectal temperature 41.5 deg C) was produced in groups of 20 mice by exposure at 30-40 mW/sq cm for 2 hr/day for 4, 7, 10, or 14 days before infecting the mice with a dose that yielded a 3-day survival rate of 60% in controls. The 3-day survival rate for the 4-day groups was 75% (15 mice), i.e., higher than for the controls. Again, the difference was deemed nonsignificant. The survival rates for the 10-day and 14-day groups were 30% and 5%, respectively, both significantly lower than for the controls.

Results of other tests by these investigators on rabbits and mice given whole-body hyperthermia were mentioned and referenced under Roszkowski et al. (1980a,b,c,d). They concluded that chronic exposure to nonthermal RFR (as defined) or exposure to repeated sessions of hyperthermic RFR lowers natural antibacterial resistance, suppresses nonspecific immune reactions, and increases mortality rates of rabbits and mice infected with acute S. aureus after such RFR exposure. They surmised that the chronic exposures may have been stressogenic.

CRITIQUE: Terming 5 and 15 mW/sq cm as "nonthermal" because exposure at these power densities did not yield measurable rectal-temperature increases can be misleading. Such exposure undoubtedly produced internal local SARs much higher than the whole-body values despite thermoregulation.

No mention was made about sham-exposing animals for comparison with the RFR-exposed groups. If only cage controls were used, it would be difficult to determine whether factors other than exposure influenced the results for the RFR-exposed animals.

The statistical treatment given to the survival-rate data was not discussed, so it is not clear why the higher 3-day survival rates (relative to controls) for the 6-week, 5-mW/sq cm group and the 4-day hyperthermic group were deemed nonsignificantly different from the rate for the controls. If these differences were significant, then the higher survival rate for the 6-week, 5-mW/sq cm group would be qualitatively consistent with the findings by Liddle et al. (1980, 1982), that RFR exposure of mice of comparable whole-body SARs after immunization against streptococcus pneumoniae provided at least temporary increased protection against postexposure challenge to S. pneumoniae.

Another unclear statistical point is the treatment given to the phagocytosis data. If the t-test was used and the uncertainties of the means were standard errors, then none of the differences was significant. However, if the uncertainties were standard deviations, then the t-test would show that the mean for the 6-week, 15-mW/sq cm group was also significantly larger ($p < 0.05$) than for the control group. Moreover, at either power density, the results for the 6- and 12-week groups differed significantly from each other.

In view of the questions raised above, further evaluation of the results of this paper would be difficult.

REFERENCES:

Liddle, C. G., J. P. Putnam, J. S. Ali, J. Y. Lewis, B. Bell, M. W. West, and O. H. Lewter
ALTERATION OF CIRCULATING ANTIBODY RESPONSE OF MICE EXPOSED TO 9-GHZ PULSED MICROWAVES
Bioelectromagnetics, Vol. 1, No. 4, pp. 397-404 (1980)

Liddle, C. G., J. P. Putnam, and O. H. Lewter
ENHANCED SURVIVAL OF MICE EXPOSED TO MICROWAVES FOLLOWING INFECTION WITH STREPTOCOCCUS PNEUMONIAE
Abstracts of Bioelectromagnetics Symposium, Los Angeles, CA, p. 88 (June-July 1982)

Roszkowski, W., J. K. Wremble, K. Roszkowski, M. Janiak, and S. Szmigielski
DOES WHOLE-BODY HYPERTHERMIA THERAPY INVOLVE PARTICIPATION OF THE IMMUNE SYSTEM?
Int. J. Cancer, Vol. 25, p. 289 (1980a)

Roszkowski, W., J. K. Wremble, M. Janiak, and S. Szmigielski
THE SEARCH FOR AN INFLUENCE OF WHOLE BODY MICROWAVE HYPERTHERMIA ON ANTITUMOR IMMUNITY
Clin. Exp. Oncol., in press (1980b)

Roszkowski, W., J. K. Wremble, M. Janiak, and S. Szmigielski
EFFECT OF WHOLE BODY HYPERTHERMIA AND DELAYED CUTANEOUS HYPERSENSITIVITY TO OXAZOLONE
Clin. Exp. Immunol., in press (1980c)

Roszkowski, W., S. Szmigielski, M. Janiak, J. K. Wremble, and W. Hryniewicz
EFFECT OF HYPERTHERMIA ON RABBIT MACROPHAGES
Zbl. Bakt. Hyg. Infekt., Vol. 1, No. 1 (1980d)

***

SZMIGIELSKI
ROSZKOWSKI
KOBUS
JELJASZEWICZ

/

ANTIBODY
ANTIGEN
CHRONIC
CW
HYPERTHERMIA
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
MEDICAL
MORTALITY
MOUSE
PULSED
RABBIT
RECTAL
RFR
THERMOREGULATION

//

1980
2450
0-1
5-40
2-9

///

105
Liburdy, R. P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977)

*

AUTHOR ABSTRACT: Inflammatory responses, which were induced in rats by a subcutaneous injection of sheep red blood cells (SRBC) into footpads, and in mice, by tail-vein trauma due to sequential bleeding, were observed in animals that had been pretreated with 26-MHz radio-frequency radiation (RFR) or with a frank thermal burden. Pretreatment of rats by RFR decreased the severity of SRBC-induced inflammation; averaged thickness of the footpad was less by 33.0% and 45.6%, respectively, than thickness observed in thermally treated and control animals. White blood cell (WBC) counts in RFR pretreated, tail-vein traumatized mice remained constant, in contrast to the leukocytosis that was observed in air-heated and in sham-exposed animals. Moreover, the inflammatory response in RFR-treated mice was accompanied by a well-defined but transient refractory state in the number of circulating specialized leukocytes. The 92-hour time course of the refractory state was characterized by a transient fourfold decrease of lymphocytes and a fourfold increase of neutrophils that peaked three hours after exposure; these changes were in marked contrast to those observed in thermal and passive controls. The results indicate that RFR can attenuate an inflammatory reaction. This inhibitory property may have relevance to immunocompetency of cell-mediated immunity (CMI), since CMI responses invoke nonspecific inflammatory reactions.

**

Study Type: Immunology and Hematology, Endocrinology;
IN VIVO; RAT, MOUSE
Effect Type: (1) RFR-induced suppression of inflammation response from injection of sheep red blood cells in rats; (2) RFR-induced acute lymphopenia and acute neutrophilia in tail-vein traumatized mice
Frequency: 26 MHz
Modulation: CW
Power Densities: E = 5780 V/m; H = 6.71 A/m; E X H = 8.62 W/sq cm
SAR: Rat: 23 W/kg; Mouse: 12.9 W/kg

EXPOSURE CONDITIONS: Animals in perforated lucite cages were sham-exposed or exposed to RFR with long axis parallel to the E-vector in a TEM cell for 4 to 7 min to induce 2-4 deg C increase of body temperature. Other animals were heated in a vented, dry-air oven at 79 deg C for 8 to 12 min to match the RFR-induced body temperature increases.

OTHER INFORMATION: Unsensitized rats were injected subcutaneously with sterile, sheep red blood cells (SRBC) in a left footpad and with saline in the contralateral footpad. Immediately after injection, groups of rats were exposed to 26-MHz RFR at 8.62 W/sq cm (SAR 23 W/kg) for 4-7

min or to dry air in a ventilated oven at 79 deg C for 8-12 min so as to obtain comparable increases in rectal temperature (2-4 deg C). Other similarly injected rats were sham-exposed as controls. Footpad swelling was scored as the increase in dorsal-ventral thickness. Four hr after such treatments, the SRBC-injected footpads of the sham-exposed rats exhibited a mean thickness increase of about 0.23 cm as compared with about 0.01 cm for the saline-injected footpads of the same rats. However, the SRBC- injected footpads increased only about 0.18 cm for the rats treated with warm air, and about 0.10 cm for the RFR-exposed rats. (The saline-injected footpads for these two groups showed mean thickness increases comparable to that for the sham-exposed group.) Thus, both RFR exposure and warm-air treatment yielded significant suppression of the SRBC-induced inflammatory response, but suppression was greater for the RFR. Twenty-four hr after injection, the footpads of all the rats returned to initial thickness.

Inflammatory responses were induced in mice by incision across the lateral vein at the distal end of the tail. Lymphocyte, neutrophil, and total leukocyte counts were obtained immediately before, and at regular intervals after, sham-exposure, RFR exposure at 8.62 W/sq cm (SAR 12.9 W/kg), or warm-air treatment to produce comparable rectal temperature increases. Both sham-exposure and warm-air treatment yielded significant leukocytosis, from about 7,000 cells/cu cm initially to 15,000 at 12 hr, which persisted for about 96 hr. Differential counts of circulating lymphocytes and neutrophils showed that both had increased about twofold, with no significant differences between the two treatments. By contrast, pronounced lymphopenia and complementary neutrophilia that summed to a substantially constant total leukocyte count of about 10,000 cells/cu cm over the 96-hr period were obtained for the RFR-exposed mice. Maximum lymphopenia and neutrophilia (both fourfold changes from initial values) occurred 3 hr after treatment, followed by gradual diminution of both effects during the remainder of the period.

The investigator suggested that the time course of lymphopenia and neutrophilia induced by the thermogenic RFR is similar to that obtained by administration of adrenocorticotropic hormones, and indicated that Lotz and Michaelson (1975) and Guillet et al. (1975) had shown that exposure of rats to RFR at levels sufficient to increase rectal temperature by 1-3 deg C led to rapid, transient increases in levels of plasma corticosterone. In a subsequent investigation with mice (Liburdy, 1979), he experimentally verified this hypothesis.

Regarding the relatively mild suppression of the inflammation response in rats to SRBC by warm-air treatment, Liburdy indicated that the effect is most likely due to peripheral vasodilation, leading to increased egress of SRBC from tissues. He ascribed the more severe suppression by RFR exposure partly to vasodilation, but also to the release of corticosterone, implying that the lymphopenia and neutrophilia observed in the mice had also occurred in the rats. In his later investigation (Liburdy, 1979), he experimentally demonstrated that delayed-type hypersensitivity (DTH) to SRBC in mice was suppressed by exposure to thermogenic RFR.

CRITIQUE: Perhaps the only important gap in this well conceived and executed investigation was experimental confirmation that the rats exposed to thermogenic RFR did indeed undergo lymphopenia and neutrophilia. However, there is no evidence that these effects did not occur.

In a still later paper (Liburdy, 1980), experimental evidence was presented that thermogenic RFR alters lymphocyte circulation among the lung, spleen, and bone marrow, and that qualitatively similar effects were obtained in steroid-injected mice.

From the information provided in the paper it is not possible to verify that the E cross H product in free space corresponds to the stated power density of 8.62 W/sq cm. Power densities reported in Liburdy (1979) are an order of magnitude lower (800 mW/sq cm). SAR values for mice per mW/sq cm incident also differ by a factor of 4.7.

REFERENCES:

Guillet, R., W. G. Lotz, and S. M. Michaelson
TIME COURSE OF ADRENAL RESPONSE IN MICROWAVE EXPOSED RATS
Abstracts of 1975 URSI International Symposium, Boulder, Colorado, p. 316 (1975)

Liburdy, R.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

Liburdy, R.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)

Lotz, W. G. and S. M. Michaelson
ADRENOCORTICAL RESPONSE IN RATS EXPOSED TO MICROWAVES
Abstracts of 1975 URSI International Symposium, Boulder, Colorado, p. 139 (1975)

***

LIBURDY

/

ANTIGEN
CORTICOSTEROID
CW
ENDOCRINOLOGY
HYPERTHERMIA
IMMUNOLOGY
INFLAMMATION
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MOUSE
RAT
RECTAL
RFR

//

1977
26
1
8620
12.9-23

///

106
Smialowicz, R. J., C. M. Weil, J. B. Kinn, and J. A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a)

*

AUTHOR ABSTRACT: Four experiments were performed in which six pregnant rats were exposed from day 12 of pregnancy to parturition, for 4 hours a day in a temperature-controlled environment, to 425-MHz (CW) radiation, using a multimode rectangular strip transmission line. Four male pups born to each dam were subsequently irradiated under the same RF exposure condition for 20-21 days of age (2 pups) and 40-41 days of age (2 pups). Specific absorption rates (SARs) for rats of different ages were determined by twin-well calorimetry as well as from calculations of power measurements of incident, reflected, and transmitted energy. Values of SARs between 3.1 and 6.7 mW/g were obtained for rats so exposed at 425 GHz. At selected times, rats were weighed to determine if the irradiation affected growth. Two rats from each litter (4 pups) were euthanized at 20-21 and two at 40-41 days of age and blood was obtained for complete blood counts. The in vitro blastogenic response of blood and lymph-node lymphocytes was measured by H-3 thymidine incorporation into DNA following stimulation of cells with T- or B-lymphocyte mitogens.

No difference was observed in the weights of irradiated compared with sham-irradiated rats. No consistent changes in the peripheral blood picture was observed between irradiated and sham-irradiated rats. Significant increases in the response of lymph-node but not of blood lymphocytes from irradiated rats following stimulation with mitogens was observed in two of four experiments. These changes were observed for both T- and B-lymphocytes.

In another experiment at the same frequency, six pregnant rats were irradiated for 16 hours daily from day 6 through day 19 of pregnancy. The pups born to these dams were not subsequently irradiated. These rats, born to irradiated dams, showed a similar increased response of node but not of blood lymphocytes to T-cell mitogens at 42 days of age. These results indicate that exposure to 425-MHz radiation, under the conditions described, may lead to increased responsiveness of node lymphocytes to in vitro stimulation by mitogen.

**

Study Type: Immunology and Hematology, Physiology and Biochemistry, Teratology and Developmental Abnormalities; IN VIVO; RAT
Effect Type: Alterations of weight, hematologic, and mitogen-stimulated lymphocyte responses in rat pups exposed to RFR perinatally
Frequency: 425 MHz
Modulation: CW
Power Densities: Not specified; forward power of 6.6 or 20 W
SAR: 3.1 to 6.7 W/kg at 20 W

EXPOSURE CONDITIONS: In 4 experiments, 6 pregnant rats were exposed concurrently in individual acrylic cages within a TEM cell at 22 deg C for 4 hr/day on gestational day 12 through parturition. Four male pups per litter were then exposed concurrently in subdivided acrylic cages at 26.7 deg C for 14 days postpartum and subsequently at 22 deg C. In experiments 1, 2, and 3, the pregnant dams and subsequently the pups were exposed at 20 W forward power. In experiment 4, the dams were exposed at 6.6 W (inadvertently), but the pups were exposed at 20 W. At age 20-21 days, 2 pups per litter were withdrawn and the remaining pups were exposed for 20 additional days. In a fifth experiment, pregnant rats were exposed for 16 hr/day from gestational day 6 to 19 at 20 W, and the pups were not exposed. Although the exposure chamber was a TEM cell, the presence of the TE01 mode at 425 MHz was detected, so the RFR was not planewave; hence, the power density concept is not applicable. Equal numbers of dams and pups were sham-exposed.

OTHER INFORMATION: Whole-body SARs were determined by twin-well calorimetry on animal carcasses and from measurements of incident, reflected, and transmitted powers in the TEM line with live animals present. The mean SARs for the two methods were in reasonable agreement. In a sample of pregnant rats, RFR exposure did not elevate colonic temperature. Pup body masses of RFR- and sham-exposed rats, measured periodically, showed no significant differences at each age.

In experiments 1-4, 2 pups (of 4) per litter at age 20-21 days and the remaining pups at age 40-41 days were bled and euthanized. Blood samples were assayed for erythrocyte count, total and differential leukocyte counts, mean cell volume of erythrocytes, hematocrit, and hemoglobin concentration. Analysis of variance was used, but to avoid false positive results, Bonferroni's Inequality was applied, i.e., the usual $p < 0.05$ criterion for significance was divided by 8, the number of independent blood-parameter analyses, to yield $p < 0.006$ as the criterion for significance. At the $p < 0.05$ level, there was an increase in the percentage of lymphocytes and decreases in the percentage and absolute number of neutrophils for the age 40-41-day RFR-exposed rats in experiments 2 and 4, but those differences were not significant at the $p < 0.006$ level. (However, note in Table 3 that the relative neutropenia in experiment 2 was labeled significant at the latter level. Also, although there was an increase in lymphocyte percentage, in this experiment, for 40-41-day rats as mentioned, the lymphocyte percentage decreased in the 20-21-day rats, at the $p < 0.05$ level.)

Cultures of blood and lymph-node lymphocytes from experiments 1-4 were stimulated with the T-cell mitogens phytohemagglutinin (PHA), concanavalin A (Con A), or the B-cell mitogens lipopolysaccharide (LPS) of E. Coli, purified protein derivative of tuberculin (PPD), or the nonspecific pokeweed mitogen (PWM), each in several concentrations. Tritiated thymidine was added to each culture 24 hr before harvesting and its uptake in DNA was determined by liquid scintillation counting as a measure of cell proliferation. Data in counts per min (CPM) were log-transformed to better satisfy the normality assumption in analysis

of variance. However, because of considerable variability among rats, two conservative tests were used to eliminate outliers; 28 of 2856 data points were thereby excluded. Results were presented as means and standard errors of nontransformed data, but significance ($p < 0.05$) was determined from the transformed data by analysis of variance.

In experiments 1 and 2 (Table 4), the results for the RFR-exposed pups showed consistently significant increases in stimulated lymph-node lymphocytes for all the mitogens, but no significant changes for the blood lymphocytes. Also, none of the unstimulated cultures yielded significant differences between RFR- and sham-exposed pups. However, the results for experiment 3 (replicate of experiments 1 and 2) showed no significant differences in lymph-node lymphocytes between the RFR- and sham-exposed rats; the only significant result was an increase of PHA-stimulated blood lymphocytes for the 40-41-day pups (Table 5). The results for experiment 4 (Table 5), in which the dams were exposed inadvertently at the lower forward power, were similar to those of experiment 3 (but at twice the PHA concentration and at a significance level $p < 0.10$).

In experiment 5 (RFR exposure of dams only), there were no significant ($p < 0.05$) differences in peripheral blood counts for the pups at age 22 or 42 days (Table 6). The only significant mitogen-stimulation results were increases of PHA- and Con A-stimulated lymph-node lymphocytes at age 42 days (Table 7).

CRITIQUE: For unstated reasons, many of the results for the 20-22-day pups were not presented, specifically: the peripheral blood counts and mitogen-stimulated peripheral-blood and lymph-node lymphocyte responses in experiment 1, and the blood-lymphocyte responses in experiments 2-5. Also, it is not clear whether stimulation with some of the mitogens was not done in some cases or whether some of the results were omitted; for example, only one subset each from Tables 5 and 7 (experiments 3 and 5) showed results for all 5 mitogens.

The investigators reported that they found variability in in-vitro mitogen-stimulated responses among animals and between similar experiments, and that they endeavored to minimize the influence of such variations on the findings by use of appropriate statistical techniques, a valid procedure. However, it is clear that the variability was too large, in most cases, for such statistical techniques to be effective. For example, note that for the 40-41 day pups in experiment 2 (Table 4), PWM stimulation of the lymph-node lymphocytes from the sham-exposed rats yielded the same mean CPM value as for the unstimulated sham-exposed rats. This could lead to the conclusion that no PWM stimulation would occur without previous RFR exposure, or conversely, that prior RFR exposure had fostered PWM stimulation. However, in experiments 3 and 5 (Tables 5 and 7), PWM was stimulative in the sham-exposed rats. Equally enigmatic, the results for experiment 3 (with the various mitogens) were qualitatively different from those for experiments 1 and 2 even though all three were the same in exposure and methodology, a point recognized by the investigators. For these reasons, any mitogen-stimulation

findings (positive or negative) of this investigation must be regarded as inconclusive.

There were also some inconsistencies in the peripheral-blood-count results of replicate experiments 1-3, notably the alterations of lymphocyte and neutrophil counts in experiment 2, discussed in the text, and the absence of these effects in experiments 1 and 3. Use of Bonferroni's Inequality largely removes these inconsistencies but does not afford direct comparisons with results of investigators who evaluated significance at the $p < 0.05$ level (who perhaps should have used Bonferroni's Inequality also).

However, it should be noted that the mitogen-stimulation results of this investigation were generally similar to those of a previous investigation at 2.45 GHz (Smialowicz et al., 1979a) and tend to support the conclusion from the latter that perinatal RFR exposure of rats alters their in-vitro mitogen-stimulated lymphocyte responses. In addition, unlike the earlier investigation, this study included a group of prenatally exposed pups that were not exposed postnatally (experiment 5). At age 42 days, the RFR-exposed pups yielded significantly higher ($p < 0.05$) responses to PHA- and Con A stimulation than the corresponding sham-exposed pups, an indication that prenatal RFR exposure was the major factor in such effects.

REFERENCES:

Smialowicz, R. J., J. B. Kinn, and J. A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

***

SMIALOWICZ
WEIL
KINN
ELDER

/

BIOCHEMISTRY
CW
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MITOGEN
PHYSIOLOGY
RAT
RFR
TRACER
WEIGHT

//

1982
425
1
0
3.1-6.7

///

107
Smialowicz, R. J., C. M. Weil, P. Marsh, M. M. Riddle, R. R. Rogers, and B. F. Rehnberg
BIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE OF RATS TO 970-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 2, No. 3, pp. 279-284 (1981d)

*

AUTHOR ABSTRACT: Rats (N = 16) exposed individually in circularly polarized waveguides to 970-MHz electromagnetic radiation (SAR = 2.5 mW/g, 22 h daily for 70 consecutive days) had significantly higher serum levels of triglycerides, albumin, and total protein compared with sham-irradiated controls. No difference was observed in the weights, hematologic profile, or in vitro lymphocyte responses to mitogens between these two groups. The higher serum levels of triglycerides in radiofrequency-radiation-exposed rats suggest a nonspecific stress reaction.

**

Study Type: Immunology and Hematology, Endocrinology, Physiology and Biochemistry; IN VIVO; RAT
Effect Type: RFR-induced alterations of splenic lymphocytes, hematologic indices, and blood-serum chemistry
Frequency: 970 MHz
Modulation: Not stated; presumably CW
Power Density: 7.8 mW/sq cm spatial average across waveguide
SAR: 2.5 W/kg

EXPOSURE CONDITIONS: Sixteen Wistar rats were exposed individually to circularly polarized RFR in circular waveguides for 70 consecutive days, 22 hr/day. Sixteen additional rats were sham-exposed similarly for controls. For treatment, all rats were in the same room, which was maintained at 21-24 deg C and 50-75% relative humidity.

OTHER INFORMATION: Both groups of rats were acclimated to their respective RFR- and sham-exposure waveguides for 4 weeks prior to treatment. There were no significant RFR-induced differences in mean weights of the two groups during acclimation or treatment.

Eight of the 16 rats in each group were bled on day 69 of RFR or sham exposure and the remainder on day 70. After bleeding, the rats were euthanized and their spleens were removed. A portion of each blood sample was evaluated for erythrocyte and leukocyte counts, mean cell volume of erythrocytes, hematocrit, and hemoglobin concentration. Differential counts of lymphocytes, monocytes, eosinophils, and polymorphonuclear leukocytes were also made. No significant differences between RFR- and sham-exposed groups were found for any of these indices.

Splenic-cell cultures stimulated with the mitogens phytohemagglutinin, concanavalin A, pokeweed mitogen, or E. coli lipopolysaccharide, and radiolabeled with tritiated thymidine showed no significant differences between RFR- and sham-exposed rats for thymidine incorporation into DNA.

The remainder of each blood sample was allowed to clot and the serum was removed, frozen, and shipped to an independent laboratory for standard serum chemistry analysis. The levels of glucose, blood urea nitrogen (BUN), creatinine, sodium, potassium, chloride, uric acid, calcium, phosphorus, cholesterol, triglyceride, alkaline phosphatase, aspartate transaminase (SGOT), alanine transaminase (SGPT), creatinine phosphokinase (CPK), lactic dehydrogenase (LDH), albumin, globulin and total protein. Analysis of variance of the results showed significant ($p < 0.05$) elevations of serum triglyceride, albumin, and total protein for the RFR-exposed group as compared with the sham-exposed group. In addition, the increases were correlated within individual animals. There were no significant differences between groups for the other serum components. (However, noted in their data but not discussed was that the levels of SGOT and LDH for both groups were abnormally high relative to reference values.)

The investigators noted that the higher values of albumin and total protein for the RFR-exposed rats were within the normal range for Wistar rats, but were statistically correlated with the triglyceride elevations, suggestive of a causal relationship. They indicated that the albumin and total-protein increases were difficult to explain in the absence of changes in the erythrocyte assays, and suggested that these rats may have been dehydrated. In the absence of RFR-induced changes of weight or other serum components such as glucose and cholesterol, the triglyceride elevations were also difficult to ascribe to possible differences in food intake. They did point out that stress causes increases in triglyceride levels, citing Deficis et al. (1979). The latter had found that increases in triglyceride levels were correlated with increases in serum beta-lipoprotein levels of mice exposed to 2.45-GHz RFR, and ascribed the effect to heat stress from the RFR. Smialowicz et al. (1981d) noted that a whole-body SAR of about 2.5 W/kg is approximately half the basal metabolic rate of an adult rat and is sufficient to cause a 2 deg C colonic-temperature increase in endotoxin-induced hypothermic rats (Smialowicz et al., 1980); they concluded that the rats exposed to 970-MHz RFR received a thermal load.

CRITIQUE: The use of circularly polarized RFR undoubtedly minimized possible variations of whole-body SAR associated with changes in rat orientation during chronic exposure.

There seem to be two discrepancies in the presentation of the serum-chemistry results in Table 1. First, the uncertainties of the means appear to be standard errors rather than standard deviations as indicated; otherwise, analysis of variance (or use of the t-test) would yield many additional significant ($p < 0.05$) differences in mean values between the RFR- and sham-exposed groups. Second, the results displayed

for creatinine appear to be incorrect in some aspect because otherwise the difference in means for the two groups would be highly significant instead of nonsignificant as indicated in the text. However, these discrepancies do not alter any of the findings of this investigation.

The negative findings for the hematologic indices and the mitogen-stimulated splenic-cell cultures are consonant with the results of previous studies with rats at 2.45 GHz and 100 MHz by this group (Smialowicz et al., 1979a, 1981b). The suggested association of the elevated serum levels of triglycerides, albumin, and total protein with heat stress from RFR absorption is supported by the results of Deficis et al. (1979) with mice, as indicated by Smialowicz et al. (1981d). At 970 MHz, there probably were regions within the rat where the local SARs were much larger than the mean whole-body SAR of 2.5 W/kg, and such higher values could have affected the endocrinological system of the rat in a manner analogous to that found by Lotz and Michaelson (1978). However, further work would be necessary to test this hypothesis and to determine the mechanisms involved.

REFERENCES:

Deficis, A., J. C. Dumas, S. Laurens, and G. Plurien
MICROWAVE IRRADIATION AND LIPID METABOLISM IN MICE
Radio Sci., Vol. 14, No. 6S, pp. 99-101 (1979)

Lotz, W. G. and S. M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHIPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respirat. Environ. Exercise Physiol., Vol. 44, No. 3 (1978)

Smialowicz, R. J., J. B. Kinn, and J. A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Smialowicz, R. J., K. L. Compton, M. M. Riddle, R. R. Rogers, and P. L. Brugnolotti
MICROWAVE RADIATION (2450 MHZ) ALTERS THE ENDOTOXIN-INDUCED HYPOTHERMIC RESPONSE OF RATS
Bioelectromagnetics, Vol. 1, No. 4, pp. 353-361 (1980)

Smialowicz, R. J., J. S. Ali, E. Berman, S. J. Bursian, J. B. Kinn, C. G. Liddle, L. W. Reiter, and C. M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)

***

SMIALOWICZ
WEIL
MARSH
RIDDLE
ROGERS
REHNBERG

/

BIOCHEMISTRY
CW
ENDOCRINOLOGY
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LEUKOCYTE
LYMPHOCYTE
MITOGEN
PHYSIOLOGY
RAT
RFR
STRESS
TRACER
WEIGHT

//

1981
970
1
7.8
2.5

///

108
Smialowicz, R. J., J. S. Ali, E. Berman, S. J. Bursian, J. B. Kinn, C. G. Liddle, L. W. Reiter, and C. M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)

*

AUTHOR ABSTRACT: A multidisciplinary approach was employed to assess the possible biological effects of chronic exposure of rats to 100-MHz continuous wave (CW) radiofrequency (RF) radiation. A group of 20 time-bred rats were exposed in a transverse electromagnetic mode (TEM) transmission line to 100 MHz at a forward power of 500 W (46 mW/sq cm) starting on Day 6 of gestation under controlled temperature and humidity conditions. Pregnant dams and later their offspring were exposed daily for 4 hr for up to 97 days of age. An equal number of sham-exposed animals, maintained under the same environmental conditions, served as controls. Specific absorption rates (SARs) for rats of varying ages were determined by twin-well calorimetry. The average SAR for all rats used in the twin-well calorimetry measurements was calculated to be 2.8 plus or minus 1.5 mW/g (mean plus or minus SD). Between exposures, animals were evaluated using various developmental and biological indices.

No difference was observed between 100-MHz-exposed and sham-exposed rats for complete blood counts, mitogen-stimulated response of lymphocytes, frequency of T- and B-lymphocytes, or antibody response to Streptococcus pneumoniae capsular polysaccharide. No mutagenic effect on the sperm cells of rats exposed for over 90 days to 100 MHz was observed using the Dominant-Lethal Assay. The mean time to eye opening was significantly accelerated in exposed compared to sham-exposed rats; however, no other significant difference in neurological development was observed. In rats exposed to 100 MHz, significant decreases in the activity of acetylcholinesterase was observed in the striatum and medulla oblongata of 22-day-old rats and in the midbrain of 40-day-old rats but not in 97-day-old animals.

**

Study Type: Immunology and Hematology; Mutagenesis, Carcinogenesis, and Cytogenetic Effects; Teratology and Developmental Abnormalities; Physiology and Biochemistry; Nervous System; IN VIVO; RAT
Effect Type: Effects of prenatal and postnatal RFR exposure on: growth, neurological development, hematology, in-vitro response of lymph-node and blood lymphocytes to mitogen stimulation, percentages of lymphoid CR+ and theta+ cells, antibody response to S. pneumoniae, sperm mutagenesis, regional brain weights, and regional brain AChE activity.
Frequency: 100 MHz
Modulation: CW
Power Density: 46 mW/sq cm
SAR: 2.8 W/kg

EXPOSURE CONDITIONS: Twenty Sprague-Dawley (CD) pregnant rats in individual acrylic cages were concurrently exposed for 4 hr/day to 100-MHz RFR in a transverse electromagnetic mode (TEM) cell at a forward power of 500 W (46 mW/sq cm) under controlled temperature and humidity until parturition. Following birth, 4 male pups per litter were similarly exposed in partitioned acrylic cages until age 20-22 days. Two pups per litter were then removed for tests and the remaining pups were exposed until 40-42 days old; at this time 1 pup per litter was removed and the others were exposed until 97 days old. Equal numbers of rats were sham-exposed for controls.

OTHER INFORMATION: The frequency selected (100 MHz) is in the band used for FM broadcasting, which was found to be a major contributor to urban environmental levels of RFR. At this frequency, which is close to the free-space resonance region for humans, the SAR for humans is in the 2-3 W/kg range for 10 mW/sq cm. Calorimetric measurements showed some SAR variations among concurrently exposed rats in the TEM cell, but an incident power density of 46 mW/sq cm was found to yield mean SARs ranging from 2.02 W/kg for pregnant rats to 2.96 W/kg for neonates, with intermediate values for the older pups.

Twenty time-bred CD rats in individual acrylic cages were concurrently exposed at 46 mW/sq cm for 4 hr/day on day 6 of pregnancy through parturition. The cages were then divided into 4 compartments, and 4 male pups per litter were randomly selected and exposed for 4 hr/day at the same power density until age 20-22 days. At this time, 2 pups per litter were removed for tests and the others were exposed until 40-42 days old. One pup per litter was then removed for tests, and the others were exposed until 97 days old. Equal numbers of rats were sham-exposed.

As an indicator of growth, body weights of the rat pups were measured periodically until age 92 days. The mean weights of the RFR-exposed animals were consistently but nonsignificantly ($p > 0.05$) higher than for the sham-exposed rats at corresponding ages, except at age 28 days, for which the difference was statistically significant.

Two pups per litter were tested for neurological development as indicated by the ages for the appearance of startle response and righting reflex, and for age of complete opening of both eyes. In addition, 1 pup per litter at ages 35 and 84 days was tested for locomotor activity in a maze. No significant differences between RFR- and sham-exposed pups were seen in these tests except for age of eye opening, which occurred at a mean age of 15.4 days for the RFR-exposed rats and at 16.0 days for the controls. The difference is not RFR-related, because the age of eye opening for control CD-strain rats in investigations of effects of other agents was found to be 15 days.

At ages 22 and 42 days, blood samples were taken and given standard hematologic tests. To determine the in-vitro response to mitogen stimulation, samples of lymph-node and blood lymphocytes were cultured with the T-cell mitogens phytohemagglutinin (PHA) or concanavalin A (Con

A), or with the B-cell mitogens lipopolysaccharide (LPS) or purified protein derivative (PPD) of tuberculin. Twenty-four hr before harvesting, cell cultures were radiolabeled with tritiated thymidine, and the incorporation of thymidine into DNA as a measure of blastogenic response was determined, after harvesting, by liquid scintillation counting. Hemograms for the 42-day-old rats showed no significant differences between RFR-exposed and control groups for any of the parameters measured. Negative results (not included) were also reported for the 22-day-old rats. No significant differences between RFR-exposed and control groups were found for any of the mitogen-stimulated cultures. Note that Table V also shows results (negative) for PWM (presumably pokeweed mitogen, a stimulant for both T- and B-cells), which was not mentioned in the text.

The percentages of complement-receptor-positive (CR+) B-cells in rat lymph nodes were determined by rosette formation with sheep erythrocytes. Lymphocytes having 3 or more adherent erythrocytes were scored as CR+ cells. Also, the percentages of thymus-derived (theta+) T-cells were determined by a cytotoxicity assay. For the 42-day-old rats, there were no significant differences, between RFR-exposed and control rats, in mean percentages of either CR+ or theta+ cells.

The primary antibody response to Type III pneumococcal polysaccharide (PPS) was determined by immunizing 22-day-old pups with PPS and assaying blood samples taken 5 days later for serum antibody titers. Again, no significant differences were obtained.

The Dominant Lethal Assay was used to determine whether the RFR exposure was mutagenic to sperm cells. At age 90 days, each RFR- and sham-exposed rat was mated with 2 virgin (unexposed) females for 1 week. Eleven days after mating, the numbers of pregnancies, live and dead conceptuses, corpora lutea, and preimplantation losses were counted. No significant differences in these endpoints were found between the female group (37 rats) mated with the 20 RFR-exposed males and the group (36 rats) mated with the 20 sham-exposed males.

At 22, 40, and 97 days of age, rats were euthanized. Their brains were removed and regionally dissected into striatum, hypothalamus, hippocampus, cortex, cerebellum, midbrain, and medulla oblongata. These regions were weighed and assayed for protein concentration and acetylcholinesterase (AChE) activity. The investigators stated that the only regional mean weight difference was for the medulla of the 40-day-old rats, which was significantly higher for the RFR-exposed than the sham-exposed rats. However, the data in Table IX shows this to be true for the cerebellum as well. There were no significant differences in regional brain protein concentrations at any age. However, striatal and medulla AChE activities were significantly depressed in the 22-day-old RFR-exposed rats, and midbrain AChE activity was depressed in the 40-day-old RFR-exposed rats.

CRITIQUE: As indicated by the investigators, this study was undertaken to determine whether chronic exposure of rats to a frequency in the FM-broadcast band (100 MHz) would significantly affect any of the biological endpoints considered. Whole-body SARs in the range 2-3 W/kg were used, this range being approximately the same as for humans exposed to this frequency at 10 mW/sq cm, the then prevailing American National Standards Institute (ANSI) maximum exposure limit (1974). The new limit at this frequency is 1 mW/sq cm (ANSI, 1982).

Almost all of the results were negative and were consonant with those obtained by Smialowicz et al. (1979a) in a similar investigation with rats chronically exposed for 4 hr/day to 2.45-GHz RFR at 5 mW/sq cm. The corresponding SARs ranged from 0.7 to 4.7 W/kg, depending on age-related weight. It is interesting to note that this SAR range is much wider than for 100 MHz, presumably because spatial variation of RFR absorption is smaller at the lower frequency.

Among the few positive results obtained by Smialowicz et al. (1981b) were significantly higher weights of the medulla and cerebellum for the RFR-exposed than the sham-exposed rats, but only at age 40 days. The other positive results were depressions of AChE activity, by RFR exposure, in the striatum and medulla at age 22 days and in the midbrain at 40 days. As pointed out by the investigators, Baranski and Edelwejn (1975) reported reductions of AChE activity in the cortex, diencephalon, mesencephalon, metencephalon, and cerebellum of rabbits chronically exposed to 2.95-GHz RFR for 2 hr/day at 5 mW/sq cm. However, Olcerst and Rabinowitz (1978) reported that in-vitro exposure of purified AChE in aqueous solution to 2.45-GHz RFR produced no significant changes in AChE activity up to 100 mW/sq cm; at 125 mW/sq cm a significant decrease in activity was seen, probably associated with temperature elevation to 60 deg C, which was sufficient to denature the enzyme.

REFERENCES:

ANSI (American National Standards Institute), C95.1-1974
SAFETY LEVEL OF ELECTROMAGNETIC RADIATION WITH RESPECT TO PERSONNEL
published by the Institute of Electrical and Electronics Engineers, New York (1974)

ANSI (American National Standards Institute), C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
published by the Institute of Electrical and Electronics Engineers, New York (1982)

Baranski, S. and Z. Edelwejn
EXPERIMENTAL MORPHOLOGIC AND ELECTROENCEPHALOGRAPHIC STUDIES OF MICROWAVE EFFECTS ON THE NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 109-116 (1975)

Olcerst, R. B. and J. R. Rabinowitz
STUDIES ON THE INTERACTION OF MICROWAVE RADIATION WITH CHOLINESTERASE
Radiat. Environ. Biophys., Vol. 15, pp. 289-295 (1978)

Smialowicz, R. J., J. B. Kinn, and J. A. Elder
PERINATAL EXPOSURE OF RATS TO 2450 MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

***

SMIALOWICZ
ALI
BERMAN
BURSIAN
KINN
LIDDLE
REITER
WEIL

/

ANTIBODY
ANTIGEN
BIOCHEMISTRY
CHRONIC
COMPLEMENT
CW
CYTOGENETIC
DEVELOPMENT
EMBRYO
HEMATOLOGY
IMMUNOLOGY
IN-VIVO
LYMPHOCYTE
MITOGEN
MUTAGENIC
NERVOUS-SYSTEM
PHYSIOLOGY
RAT
RFR
TRACER
TERATOGENIC
WEIGHT

//

1981
100
1
46
2.8

///

109
Lin, J.C. and M.F. Lin
STUDIES ON MICROWAVE AND BLOOD-BRAIN BARRIER INTERACTION
Bioelectromagnetics, Vol. 1, No. 3, pp. 313-323 (1980)

*

AUTHOR ABSTRACT: This investigation was aimed at correlating changes of blood-brain-barrier permeability with the quantity and distribution of absorbed microwave energy inside the brain of adult Wistar rats anesthetized by sodium pentobarbital. Through use of thermographic methods and a direct-contact applicator at the animal's head, the pattern of absorbed microwave energy was determined. Indwelling catheters were placed in the femoral vein and in the left external carotid artery. Evans blue and sodium fluorescein in isotonic saline were used as visual indicators of barrier permeation.

Exposure to pulsed 2,450-MHz radiation for 20 min at average power densities of 0.5, 1, 5, 20, 145, or 1,000 mW/sq cm, which resulted in average specific absorption rates (SARs) of 0.04, 0.08, 0.4, 1.6, 11.5, or 80 mW/g in the brain, did not produce staining, except in the pineal body, the pituitary gland, and the choroid plexus--regions that normally are highly permeable. Except for these regions, staining was also absent in the brains of sham-exposed animals. The rectal temperature, as monitored by a copper-constantan thermocouple, showed a maximum increase of less than 0.75 deg C from a mean pre-exposure temperature of 36.6 deg C. The highest brain temperature recorded in a similar group of animals using a thick-film carbon thermistor was less than 41.0 deg C.

**

Study Type: Nervous System; IN VIVO; RAT
Effect Type: RFR-induced increases of the blood-brain-barrier permeability to Evans blue dye or sodium fluorescein
Frequency: 2.45 GHz
Modulation: 10-microsecond pulses at 25 or 50 pps; 20-microsecond pulses at 100 or 500 pps
Power Densities: 0.5-1000 mW/sq cm Av, 2-100 W/sq cm Pk, calculated from average forward and reflected powers, duty cycles, and aperture area
SAR: 0.04-80 W/kg Av, 160-8000 W/kg max, in the brain

EXPOSURE CONDITIONS: Anesthetized rats were locally exposed with a small (14-mm-diam-aperture) dielectrically loaded applicator in contact with the left side of the head for 20 min. Control rats were sham-exposed.

OTHER INFORMATION: Distributions of energy absorption in the heads of rat carcasses were determined by scanning infrared thermography over horizontal and parasagittal planes, and local temperature increases produced by brief exposure to a high level of CW RFR were used to

calculate local SARs. The results indicated that the energy was deposited largely in the left hemisphere, with a maximum SAR of 55 W/kg per watt in the cortical region, a value that is equivalent to 0.08 W/kg per mW/sq cm.

Rectal temperatures were monitored with a thermocouple. Also, the temperature in the cerebral cortex was monitored continuously in a separate group of rats with an indwelling thick-film carbon thermistor probe. For SARs up to 0.4 W/kg, the increases in cortical temperature were smaller than the rectal temperature increases and vice versa for higher SARs. At 1.6, 11.5, and 80 W/kg, the differences between cortical and rectal temperatures were about 0.2, 0.5, and 4.0 deg C, respectively. At 80 W/kg, the cortical temperature rose to over 40 deg C (80% of the increase, not 80% of the final value as stated in the text) during the first 3 min, and rose more slowly to 41.0 deg C during the remaining 17 min.

Prior to RFR- or sham exposure, a polyethylene catheter was implanted in the femoral vein or the left external carotid artery or both. In most experiments, Evans blue dye or the tracer sodium fluorescein was administered via the femoral vein immediately after exposure. For rats injected with the dye, each rat was euthanized shortly afterward and the brain was perfused with saline until the eyes and forepaws were clear of pigment. The brain was then quickly removed, examined for gross alterations, frozen, and sectioned. Two investigators graded the sections by light microscopy for extravasated dye on a scale of 0 to 4+. Rats injected with fluorescein were similarly treated and graded by fluorescence microscopy. For positive controls, hypertonic urea was infused through the carotid catheter (in lieu of RFR- or sham exposure) and 1 min later, Evans blue dye was injected via either catheter.

The results with urea and Evans blue dye showed extensive unilateral staining in brain regions normally supplied by the left carotid artery. Such staining was evident (graded 2+ to 4+) in the cerebral cortex, hippocampus, caudate nucleus, thalamus, and hypothalamus of 5 of the 7 rats used. By contrast, only 1 of 36 brains exposed at any of the 6 RFR levels (0.04 to 80 W/kg average SAR) exhibited staining in these regions, graded 2+. This occurred for exposure at 0.08 W/kg average, 160 W/kg maximum SAR. Sham- and RFR exposure did yield staining in the pineal body, pituitary gland, and choroid plexus--regions in which capillaries are known to be leaky.

In the experiments with the tracer sodium fluorescein, the brains of the 3 rats infused with urea showed ipsilateral fluorescence (graded 2+ to 4+) in the same regions as with the dye, but no signs of extravasation were evident in the 16 brains exposed at any of the 4 RFR levels (0.08 to 11.5 W/kg average) or in the 4 sham-exposed brains.

CRITIQUE: The investigators pointed out that their negative results on BBB disruption at such high RFR levels (up to average power densities of 1000 mW/sq cm and local SARs of 80 W/kg) may seem unusual, but they correctly emphasized that their reported SARs, done with rat carcasses,

represent indices of field strengths rather than of thermal energy in the brain of the living animal. The sharp rise of the in-vivo brain temperature to over 40 deg C and subsequent slow rise to 41 deg C during 20 min of exposure at 80 W/kg is an indication of thermoregulation and transfer of much of the heat generated locally to unexposed parts of the body by blood circulation. In the same context, local exposure with an applicator is far different from whole-body exposure with plane-wave RFR, so citing average power densities (e.g. 1000 mW/sq cm) may be misleading. Instead, the brain temperature attained by RFR exposure may be a better basis for comparing results.

Thus, Lin and Lin indicated that their results are consonant with those of Sutton et al. (1973) and Sutton and Carroll (1979), who showed that to increase the BBB permeability of the rat to horseradish peroxidase with RFR, the brain temperature must be raised above 42 deg C for appreciable durations. Lin and Lin also pointed out that Merritt et al. (1978) obtained reliable increases of fluorescein and C-14 mannitol uptake in the rat brain only in rats rendered hyperthermic with RFR.

It is interesting that the results of Lin and Lin were obtained with pulsed RFR of duty cycles ranging from 0.01 to 0.00025, indicating that the BBB of the rat is not disrupted by high-level RFR pulses per se.

REFERENCES:

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

Sutton, C.H., R.L. Nunnally, and F.B. Carroll
PROTECTION OF THE MICROWAVE-IRRADIATED BRAIN WITH BODY-CORE HYPOTHERMIA
Cryobiology, Vol. 10, pp. 513-514 (1973)

***

LIN

/

BBB
HYPERTHERMIA
IN-VIVO
NERVOUS-SYSTEM
PULSED
RAT
RFR
THERMOREGULATION
TRACER

//

1980
2450
0.00025-0.01
0.5-1000
0.04-80

///

110
Preston, E., E.J. Vavasour, and H.M. Assenheim
PERMEABILITY OF THE BLOOD-BRAIN BARRIER TO MANNITOL IN THE RAT FOLLOWING 2450 MHZ MICROWAVE IRRADIATION
Brain Res., Vol. 174, pp. 109-117 (1979)

*

AUTHOR ABSTRACT: The radiotracer method of Oldendorf was used to determine if 2450 MHz continuous wave (CW) microwave energy increases blood-brain barrier permeability to C-14 mannitol, which is normally excluded from entering the brain. Anesthetized, adult rats were irradiated singly for 30 min in the quiet zone of an anechoic chamber, at average power densities from 0.1 to 30 mW/sq cm. Afterwards each rat received an intracarotid bolus injection of C-14 mannitol/H-3 water mixture and was decapitated 15 sec later. Uptake of C-14 mannitol relative to the highly permeable reference substance, H-3 water, was calculated as the brain uptake index (BUI) for 4 brain regions.

Mean BUI values for tissues from the microwave-irradiated rats did not differ significantly from sham-irradiated animals, and a microwave influence on barrier permeability was not evident. Irrespective of treatment, BUI values for cerebellum and medulla were much higher and more variable than values for cortex or diencephalon, and were associated with reduced absorbance or retention of H-3 water. Because of a compromising influence of the vertebral arterial supply on the distribution of intracarotid-injected radiotracers, BUI measurements in caudal brain regions are probably unreliable unless accompanied by data on regional radioisotope concentrations. The absence of such data in an earlier BUI study, suggests that increases in BUI for cerebellum and medulla attributed to microwaves were possibly misinterpreted as differences in barrier permeability to C-14 saccharides, when in fact changes in blood flow and H-3 water influx or egress were responsible.

**

Study Type: Nervous System; IN-VIVO; RAT
Effect Type: RFR-induced disruption of the blood-brain barrier as detected by radiolabeled mannitol in the parenchyma of various brain regions
Frequency: 2.45 GHz
Modulation: CW
Power Densities: 0.1 to 30 mW/sq cm
SAR: not measured

EXPOSURE CONDITIONS: Anesthetized rats were exposed individually for 30 min to 0 (sham), 0.1, 0.5, 1, 5, or 10 mW/sq cm in series 1 or to 0, 0.3, 1, 3, 10, or 30 mW/sq cm in series 2. Exposures were done in the far field of a horn within an anechoic chamber at an ambient temperature of 22 deg C, with the rat facing the horn, and with the E-vector vertical.

OTHER INFORMATION: Only CW RFR (2.45 GHz) was used, in contrast with the work of Oscar and Hawkins (1977), who exposed rats to pulsed or CW RFR (1.3 GHz). Rectal temperatures measured by Preston et al. before and after the 30-min exposures showed mean decreases ranging from 0.74 to 1.36 deg C for all groups except those exposed at 10 or 30 mW/sq cm; the mean temperature change was less than 0.1 deg C for the 10-mW/sq cm groups, and the 30-mW/sq cm rats exhibited a mean increase of 1.5 deg C.

Prior to RFR exposure, the left common carotid artery of each anesthetized rat was surgically exposed, and between 7 and 12 min after RFR exposure, 0.2 ml of Krebs-Ringer solution containing 1 microcurie each of C-14 mannitol and H-3 water was injected into the artery as a bolus. Fifteen seconds after injection, the rat was decapitated and the brain was removed. The cerebral cortex, diencephalon, cerebellum, and medulla (with pons) of the left (ipsilateral) half were dissected out and prepared for C-14 and H-3 assays by liquid scintillation counting. Counts per min (cpm) were corrected for quenching, and disintegrations per min (dpm) were calculated for tissue samples and the injectate. The values were used to calculate the brain uptake index (BUI) defined by:

BUI=100(tissue dpm C-14/dpm H-3)/(injectate dpm C-14/dpm H-3)

In series 1, 1 rat each was exposed at 0 (sham), 0.1, 0.5, 1, 5, or 10 mW/sq cm each day for 8 days, totaling 48 rats, and the injections were done with a 30-gauge needle. In series 2, 1 rat each was exposed at 0, 0.3, 1, 3, 10, or 30 mW/sq cm for 6 days, totaling 36 rats, and a 27-gauge needle was used (cf. Oscar and Hawkins, 1977). In a separate experiment, there were no significant differences in BUI values obtained with the two needle sizes.

The results for both series showed no significant differences ($p>0.05$, Student's t-test) in BUI values, for each brain region, between RFR- and sham-exposed rats. The mean BUI values for the cerebral cortex and diencephalon were about 22% irrespective of treatment. The mean values for the cerebellum and medulla were much higher, and there was much more variability, related to the observation that both regions contained more C-14 and less H-3 than diencephalon or cortex.

In preliminary experiments, visible staining of the brain occurred with intravenous injection of Evan's Blue dye as an indicator of blood-brain-barrier (BBB) disruption with hypertonic solutions of propylene glycol. The BUI injection- and assay methodology was then tested by injecting 60% propylene glycol into the left common carotid (in lieu of RFR exposure), followed 2 min later by the C-14 mannitol/H-3 water injectate. For controls, saline was injected instead of propylene glycol. The results showed that propylene glycol greatly increased the mannitol BUI values (relative to saline); the highest values were for the cortex and diencephalon.

An experiment was also performed to determine whether H-3 water injected intravenously would be distributed evenly in brain tissue or in the pattern obtained from intracarotid injection, i.e., highest uptake in the cerebrum and lowest uptake in the medulla. Rats were injected with 1 ml of 0.9% saline containing 10 microcuries of H-3 water. The rats were decapitated 1.5 min later, and the concentrations of H-3 in the four brain regions were assayed. The highest and lowest concentrations were in the diencephalon and cortex, respectively, but none of the differences was statistically significant. Thus, the lower H-3 concentrations seen in the cerebellum and medulla of the rats injected via the common carotid were probably related to blood flow distribution.

CRITIQUE: This investigation was directed primarily toward replicating the work of Oscar and Hawkins (1977), with negative results. Merritt et al. (1978) were also unable to obtain positive results with the same basic methodology. Moreover, both Merritt et al.(1978) and Preston et al. (1979) used positive controls (urea by the former; propylene glycol by the latter) as alternative agents to RFR, to ensure that disruption of the BBB could be detected by BUI changes.

Preston et al. (1979) suggested that during the 15-second interval between radioisotope injection and decapitation, the amount of H-3 water entering and leaving the cerebellum and medulla could depend critically on the dynamics of blood flow distribution to perfusion regions closely shared by the vertebral and carotid arteries. This suggestion is consonant with results by Oscar et al. (1979) indicating that RFR-induced blood-flow changes in the brain could yield increases in BUI not associated with BBB disruption.

REFERENCES:

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)

Oscar, K.J. and T.D. Hawkins
MICROWAVE ALTERATION OF THE BLOOD-BRAIN BARRIER SYSTEM OF RATS
Brain Res., Vol. 126, pp. 281-293 (1977)

Oscar, K.J., S.P. Gruenau, M.T. Folker, and S.I. Rapoport
LOCAL CEREBRAL BLOOD FLOW AFTER MICROWAVE EXPOSURE
Brain Res., Vol. 204, pp. 220-225 (1981)

***

PRESTON
VAVASOUR
ASSENHEIM

/

BBB
BRAIN-UPTAKE-INDEX
CW
IN-VIVO
NERVOUS-SYSTEM
POSITIVE-CONTROL
RAT
RFR
TRACER

//

1979
2450
1
0.1-30
0

///

111
Albert, E.N. and J.M. Kerns
REVERSIBLE MICROWAVE EFFECTS ON THE BLOOD-BRAIN BARRIER
Brain Res., Vol. 230, Nos. 1-2, pp. 153-164 (1981)

*

AUTHOR ABSTRACT: Low level microwave exposure of Chinese hamsters resulted in reversible permeability of the blood-brain barrier (BBB) to horseradish peroxidase (HRP). Lesions were grossly visible in random areas of the brain immediately following exposure, but were not as common following a 1 h recovery period and were absent after a 2 h recovery period. The apparent route of increased permeability was via endothelial vesicular transport, since reaction product was not seen passing through the endothelial tight junctions. In addition, endothelial flooding of HRP, platelet aggregation and perivascular edema were observed only in experimental animals. Possible mechanisms for the enhanced vesicular transport are discussed.

**

Study Type: Nervous System; IN VIVO; CHINESE HAMSTER
Effect Type: Morphological detection of RFR disruption of the blood-brain barrier with the tracer horseradish peroxidase, the most probable mechanism involved, and the reversibility of the phenomenon
Frequency: 2.45 GHz
Modulation: CW
Power Density: 10 mW/sq cm
SAR: 2.5 W/kg (calculated)

EXPOSURE CONDITIONS: Thirty-nine Chinese hamsters were exposed to far-field 2.45-GHz CW RFR at 10 mW/sq cm for 2 hr and were immediately injected with horseradish peroxidase. Twelve other hamsters were similarly exposed, but 6 were allowed to recover for 1 hr and 6 for 2 hr before injection. Equal numbers of hamsters were sham-exposed.

OTHER INFORMATION: A group of 39 hamsters was injected with the tracer protein horseradish peroxidase (HRP) immediately after RFR exposure. Five min later, each animal was perfused with the tissue fixative glutaraldehyde. The animal was kept overnight at 4 deg C, after which 100-micron slices of various brain tissues were prepared. The tissue sections were incubated in a medium containing 3,3-diaminobenzidine (DAB) and hydrogen peroxide. The reaction of DAB with HRP in the presence of hydrogen peroxide yields a dark-brown product, and visual detection of this reaction product outside the blood vessels in a brain slice is interpreted as evidence that HRP had leaked into the adjacent parenchyma. After such preparation, brain slices were evaluated by two individuals independently for grossly visible leakage with a dissection microscope; the regional frequency of the lesions and the color intensity of the reaction product were subjectively integrated and scored on a scale of 1 to 4. Lesion areas were then further trimmed, postfixed, stained, dehydrated, and embedded for light and electron

microscopy. A group of 12 other hamsters was similarly exposed to RFR but 6 were allowed to recover for 1 hr and the other 6 for 2 hr prior to fixation. Equal numbers of hamsters were sham-exposed.

Gross observations of brain slices from the first group showed the presence of reaction product in normally leaky areas of the posterior pituitary, median eminence, pineal gland, area postrema, choroid plexus, and the subfornical organ of both RFR- and sham-exposed animals. In addition, randomly distributed lesions in other brain regions were found in about a third of the RFR-exposed animals, notably in the pons, cerebellum, areas around the fourth ventricle, and thalamus, but also in the hypothalamus, hippocampus, and cerebral cortex. Some sham-exposed animals also displayed a few random lesion areas, with a slight propensity for the thalamus. In the 1-hr-recovery groups, only 2 RFR-exposed animals and 1 sham-exposed animal showed evidence of lesions in the brain stem and cerebellum. No gross lesions were evident in the 2-hr-recovery groups.

Light-microscopic examination of lesion areas showed that capillaries, venules, and some arterioles were often surrounded by reaction product. Leaky blood vessels were found to contain reaction product in the region of the basal lamina, around pericytes or smooth muscle of the microvasculature, and around nerve cell bodies. Concentration of reaction product was greatest in vascular walls and diminished with distance into the parenchyma.

Electron-microscopic examination of leaky vessels from RFR-exposed animals indicated the presence of reaction product in the vesicular structures of endothelial cells, basal lamina, and surrounding pericytes. Tight junctions between endothelial cells appeared intact in all vessels examined, and complete transendothelial channels were not seen. However, endothelial cells of RFR-exposed animals appeared to have more pinocytotic vesicles with HRP than cells of sham-exposed animals (by a factor of 2-3), so these investigators suggested that the latter is the most likely transport mechanism across the RFR-disrupted BBB.

CRITIQUE: This investigation closely resembles a previous one (Albert, 1979), in which Chinese hamsters and rats were exposed to 2.8-GHz RFR at 10 mW/sq cm for 2 hr and given the same postexposure treatments and morphological examinations. The findings of RFR-induced BBB disruptions and their reversibility in the later investigation lend greater credence to the earlier results with Chinese hamsters. However, increased BBB permeability in sham-exposed animals was found again, an indication that other factors in the experimental procedure may have contributed to the positive results. The presence of endogenous peroxidase may be one possible factor. On the other hand, Sutton and Carroll (1979) found no endogenous peroxidase in their control animals, but their experimental species (rat), exposure regimen, and HRP methodology were vastly different.

REFERENCES:
Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979)

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

***

ALBERT
KERNS

/

BBB
CW
HAMSTER
IN-VIVO
MICROSCOPY
NERVOUS-SYSTEM
RFR
TRACER

//

1981
2450
1
10
2.5

///

112
Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

*

AUTHOR ABSTRACT: In order to study the tolerance of the blood-brain barrier to microwave irradiation at 2450 MHz, and to determine the upper limits of time and temperature for application of microwaves without excessive disruption of the barrier, an experimental model was developed. The rat's head was heated selectively in the near field by shielding the remainder of the body. Brain and body-core temperatures were monitored via thermocouples. An enzymatic tracer protein, horseradish peroxidase, was administered intravenously (0.18 g/kg) 30 minutes before an animal was euthanized. Biochemical quantitation of extravasated peroxidase in homogenized brains of animals, which had been perfused through the aorta with 5% PVP in saline at 4 deg C to purge intravascular blood and tracer, was the index of barrier permeation.

In initially normothermic (37 deg C) animals, barrier integrity was diminished after heating of brains for 10 minutes at 45 deg C, after 15 minutes at 42 deg C, and after 60 minutes at 40 deg C. In precooled (30 deg C) rats, mortality and barrier integrity were diminished after heating brains for 15 minutes at 45 deg C, after 30 minutes at 42 deg C, and after 180 minutes at 40 deg C. Microwave-induced hyperthermia apparently increased the permeability of the blood-brain barrier to protein, but less so when the lower body was cooled. The tolerance of the barrier to microwave irradiation is dose-related and is dependent on the temperature to which the brain is heated and on the length of time during which that temperature is maintained. The barrier received significant protection from body-core hypothermia, probably through cooling of endothelial cells by circulating blood.

**

Study Type: Nervous System, Medical Applications; IN VIVO; RAT
Effect Type: Alterations of the blood-brain barrier by localized heating of the head with RFR, without and with concurrent systemic hypothermia
Frequency: 2.45 GHz
Modulation: CW
Power Density: Not given; 0-80 W forward power
SAR: Not measured

EXPOSURE CONDITIONS: The head of the anesthetized rat was selectively exposed to RFR with an applicator fed from a diathermy unit. The applicator was 2 cm above the scalp. A collar of RFR-absorbent material around the neck shielded the rest of the rat. An initial forward power of 80 W was applied until the desired brain temperature (measured with a thermocouple inserted through the skull) was attained, at which time the

power was reduced to maintain that temperature for the desired duration. A cooling coil was used to regulate body-core temperature.

OTHER INFORMATION: Brain temperatures, measured with a thermocouple inserted through the skull into the right cerebral hemisphere during RFR exposure, were repeatable to within 0.25 deg C and were not perturbed by the RFR when the leads were perpendicular to the E-vector. The thermal field of the applicator was visualized with an encapsulated-liquid-crystal sheet over an RFR-absorbent surface to ensure that the brain was exposed to a uniform field. Body-core temperatures were also monitored with a thermocouple during exposure, and a cooling coil was used to maintain either about 37 deg C (normothermia) or 30 deg C (hypothermia).

The heads of normothermic rats were heated with RFR and their brain temperatures were held at 40, 42, or 45 deg C for 10, 15, or 30 min. In other normothermic rats, the brain temperatures were held at 40 deg C for 45, 60, 90, or 120 min. After exposure, the rats were euthanized and their brains were removed for assay. Control rats were euthanized for assay after 10, 15, 30, or 120 min of sham-exposure. Brain temperatures of hypothermic rats were maintained at: 40, 42, or 45 deg C for 15, 30, or 45 min; 42 or 45 deg C for 10 min; 40 deg C for 60, 90, 120, or 180 min; or 45 deg C for 90 min. Control rats, with brain and body core both hypothermic, were euthanized after 180 min. Euthanizing was done by intracardial perfusion of polyvinylpyrrolidone (PVP) at mean arterial pressure for 2-5 min to clear the vascular tree of blood and peroxidase.

The circulating halftime for the tracer horseradish peroxidase (HRP) used to ascertain the condition of the blood-brain barrier (BBB) previously had been found to be about 22 min in mice, so HRP was injected either immediately before exposure into the rats exposed for less than 30 min, or 30 min before euthanizing the rats exposed for longer periods. In control experiments: heating crystalline HRP with RFR to 45 deg C for 30 min did not diminish its activity; rat brains perfused with PVP displayed no endogenous peroxidase activity; and brains of rats not exposed to RFR but perfused with HRP 30 min before euthanizing showed no peroxidase activity, confirming an intact BBB.

The left cerebral hemisphere and the cerebellum with attached brain stem of each rat were assayed for peroxidase activity by spectrophotofluorometry, and the values for the two regions were combined. (The right cerebral hemisphere was excluded because it sustained mild injury from the thermocouple.) Results were expressed in terms of micrograms of peroxidase activity per gram of brain.

The results for normothermic rats showed no significant peroxidase activity in brains heated to 40 deg C for 10, 15, or 30 min, or to 42 deg C for 10 min. However, progressively higher activities were obtained in brains heated to 40 deg C for 60, 90, or 120 min. This was also true for brains heated to 42 deg for 15 or 30 min, and for brains heated to 45 deg for 10, 15, or 30 min. By contrast, no significant peroxidase activity was evident in brains of hypothermic rats heated to

40 deg C for 60, 90, or 120 min, indicating that the hypothermia was protective of the BBB. This was true to a lesser extent for hypothermia against 42 deg C; no significant activity was obtained for 10- or 15-min exposures, but the mean activities in hypothermic and normothermic rats exposed for 30 min were comparable. Hypothermia provided little protection of the BBB at 45 deg C for exposures of 15 min or longer. However, most normothermic rats were moribund after 30 to 60 min, whereas hypothermic rats readily survived for 3 hr.

The investigators concluded that for treatment of malignant brain tumors by RFR-induced hyperthermia, the temperature of normal brain tissue should not exceed 40 deg C, and that the duration of such treatment should not exceed 30 min/session to avoid brain edema. However, systemic hypothermia concurrent with the RFR permits use of higher temperatures and longer durations.

CRITIQUE: The results of this investigation clearly demonstrate that hyperthermic levels of RFR in the brain can alter the permeability of the BBB and that the use of concurrent systemic hypothermia may permit the use of higher RFR-induced brain temperatures and longer exposure durations, in the treatment of malignant brain tumors, than without such hypothermia.

Albert (1977, 1979) suggested that endogenous peroxidase may confound results obtained with injected HRP. However, Sutton and Carroll found no endogenous peroxidase activity in control rats perfused with PVP.

Sutton and Carroll suggested that in treating patients having brain tumors in the cerebrum with RFR, it may be necessary to shield the cerebellum because BBB disruption may occur earlier in the latter than in the cerebrum, citing Albert's (1977) morphological studies of the BBB in the Chinese hamster. This suggestion is puzzling because Albert (1977) had stated: "The altered permeability of the microvasculature does not appear to be confined to any particular region of the brain."

REFERENCES:

Albert, E.N.
LIGHT AND ELECTRON MICROSCOPIC OBSERVATIONS ON THE BLOOD-BRAIN BARRIER AFTER MICROWAVE IRRADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 294-304 (1977)

Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979)

***

SUTTON
CARROLL

/

BBB
CW
HYPERTHERMIA
HYPOTHERMIA
IN-VIVO
MEDICAL
NERVOUS-SYSTEM
RAT
RFR
TRACER

//

1979
2450
1
0
0

///

113
Lin, J.C. and M.F. Lin
MICROWAVE HYPERTHERMIA-INDUCED BLOOD-BRAIN BARRIER ALTERATIONS
Radiat. Res., Vol. 89, pp. 77-87 (1982)

*

AUTHOR ABSTRACT: We have studied the interaction of microwaves with the blood-brain barrier in Wistar rats. Indwelling catheters were placed in the femoral vein. Evans blue in isotonic saline was used as a visual indicator of barrier permeation. Irradiation with pulsed 2450-MHz microwaves for 20 min at average power densities of 0.5 to 2600 mW/sq cm, which resulted in average specific absorption rates (SARs) of 0.04 to 200 mW/g in the brain, did not produce staining, except in regions that normally are highly permeable.

When the incident power density was increased to 3000 mW/sq cm (SAR of 240 mW/g), extravasation of Evans blue could be seen in the cortex, hippocampus, and midbrain. The rectal temperature, as monitored by a copper-constantan thermocouple, showed a maximum increase of less than 1.0 deg C. The brain temperature recorded in a similar group of animals using a non-field-perturbing thermistor exceeded 43 deg C. At the higher power density the extravasation depended on the irradiation and euthanization times. In one series of experiments, rats were irradiated at 3000 mW/sq cm for 5, 10, 15, and 20 min. Immediately after irradiation all except the 5-min animals exhibited increased permeability in some regions of the brain. Brains of rats euthanized 30 min after irradiation were free of Evans blue, while those euthanized 10 and 20 min postirradiation showed significant dye staining but with less intensity than those euthanized immediately after irradiation.

**

Study Type: Nervous System; IN VIVO; RAT
Effect Type: Hyperthermic-RFR-induced alterations of the blood-brain-barrier permeability to Evans blue dye
Frequency: 2.45 GHz
Modulation: 10-microsecond pulses at 500 pps; duty cycle 0.005
Power Densities: 1-3.25 W/sq cm Av, 200-650 W/sq cm Pk, calculated from average forward and reflected powers, duty cycle, and aperture area
SAR: 80-260 W/kg Av in the brain

EXPOSURE CONDITIONS: Anesthetized rats were locally exposed with a small (14-mm-diam-aperture) dielectrically loaded applicator in contact with the left side of the head. Exposures were at various average power densities up to 3.25 W/sq cm and durations up to 20 min.

OTHER INFORMATION: This investigation was an extension of the work by Lin and Lin (1980) to higher brain SARs. Distributions of energy absorption in the heads of rat carcasses had been determined by scanning infrared thermography. The maximum SAR was 55 W/kg per watt in the left cortical region, or 0.08 W/kg per mW/sq cm. Thus, for average power

densities in the range 1-3.25 W/sq cm, the corresponding SARs were 80-260 W/kg.

Rectal temperatures were monitored with a thermocouple, and presumably as in the previous investigation, cerebral-cortex temperatures were measured continuously in a separate group of rats with an indwelling thick-film carbon thermistor. During 20 min of exposure, the mean rectal temperature increased about 1 deg C for SARs of 80 to 240 W/kg (1-3 W/sq cm) and about 2 deg C for 260 W/kg (3.25 W/sq cm). The cortical temperature increases were 4 to 13 deg C for the 80- to 260-W/kg range. At 240 W/kg (3.0 W/sq cm), the cortical temperature rose to about 43 deg C during the first 3 min, and to about 44 deg C during the remaining 17 min.

Prior to RFR- or sham exposure, a polyethylene catheter was implanted in the femoral vein. In the first series, rats were exposed at 240 W/kg for 5, 10, 15, or 20 min, and injected immediately afterward with Evans blue dye via the catheter. Five min later, each rat was perfused with normal saline via the left ventricle until the eyes and forepaws were clear of pigment, at which time the rat was fixed with formalin. The brain was then removed and examined for gross staining, and 1-mm sections were cut and graded with a light microscope for staining on a scale of 0 to 6+ by two independent investigators. The grades were statistically analyzed with Student's t-test.

In the first series, the sham-exposed controls showed staining only in the pineal body, pituitary gland, and choroid plexus, regions in which capillaries are known to be leaky. The 5-min exposures yielded slight cortical staining in some rats, a result that was statistically nonsignificant ($p>0.1$) relative to controls. For the exposures of 10, 15, and 20 min, significant ($p<0.01$) and progressively greater staining was evident in the cerebral cortex, hippocampus, and midbrain.

In the second series, rats were exposed for 20 min at 80, 160, 210, 240, or 260 W/kg, and otherwise treated in the same manner as for the first series. No significant staining was seen for the SARs less than 240 W/kg. The investigators noted that the mean cortical temperature for these groups did not exceed 43 deg C. However, at 240 and 260 W/kg, unilateral hemispheric staining was evident in elements of the cerebral cortex, hippocampus, caudate nucleus, and thalamus.

In the third series, rats were exposed at 240 W/kg for 10 min, but Evans blue dye was injected 5, 10, 20, or 30 min postexposure, followed 5 min later by saline clearing and formalin fixation as before. Controls were RFR-exposed but similarly treated immediately after exposure. Progressively less staining with increasing postexposure time delay was obtained, with the 30-min group free of staining. The difference between the 5-min and control (0-min) groups was nonsignificant, but the results for the longer delays were significant at the $p<0.01$ level.

CRITIQUE: Among the three series of experiments, there was one set of common treatments: exposure at 240 W/kg for 10 min followed immediately

by injection with Evans blue (one group in the first series and the control group in the third series). From Figures 1 and 8, the mean staining scores for these two groups were approximately 2.5 and 3.0, but from the standard-deviation bar for the former (about 0.6), the difference did not appear to be statistically significant.

As in the previous investigation, the reported SARs, done with rat carcasses, represent field strengths rather than thermal energy in the brain of the living rat. A better basis for comparing results may be the brain temperature produced by RFR exposure.

The investigators confirmed and extended their findings that the BBB of the rat is not reliably disrupted by RFR exposure that increases the brain temperature to less than 44 deg C, even after 20 min of exposure. Significant dye permeation was evident at or above this critical temperature. These results are consonant with those of Sutton and Carroll (1979), who found that to increase the BBB permeability of the rat to the tracer horseradish peroxidase with RFR, it is necessary to raise the brain temperature above 42 deg C for appreciable durations. Also, Merritt et al. (1978) obtained increased BBB permeability to fluorescein and C-14 mannitol in RFR-exposed rats, but only if the rats were rendered hyperthermic.

The finding by Lin and Lin that RFR-induced BBB disruption in the rat was temporary (at the RFR levels used) was qualitatively similar to the results by Albert and Kerns (1981) in the Chinese hamster, thus providing a basis for postulating that the phenomenon may be temporary in the human brain as well. The significance of this point is the possibility of using brain hyperthermia (concurrent with systemic hypothermia) for treatment of malignant brain tumors with less likelihood of permanent BBB alteration.

REFERENCES:

Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979)

Albert, E.N. and J.M. Kerns
REVERSIBLE MICROWAVE EFFECTS ON THE BLOOD-BRAIN BARRIER
Brain Res., Vol. 230, Nos. 1-2, pp. 153-164 (1981)

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

***

LIN

/

BBB
HYPERTHERMIA
IN-VIVO
NERVOUS-SYSTEM
PULSED
RAT
RFR
TRACER

//

1982
2450
0.005
1000-3250
80-260

///

114
Ward, T.R., J.A. Elder, M.D. Long, and D. Svendsgaard
MEASUREMENT OF BLOOD-BRAIN BARRIER PERMEATION IN RATS DURING EXPOSURE TO 2450-MHZ MICROWAVES
Bioelectromagnetics, Vol. 3, No. 3, pp. 371-383 (1982)

*

AUTHOR ABSTRACT: Adult rats anesthetized with pentobarbital and injected intravenously with a mixture of C-14 sucrose and H-3 inulin were exposed for 30 min to an environment at an ambient temperature of 22, 30, or 40 deg C, or were exposed at 22 deg C to 2450-MHz CW microwave radiation at power densities of 0, 10, 20, or 30 mW/sq cm. Following exposure, the brain was perfused and sectioned into eight regions, and the radioactivity in each region was counted. The data were analyzed by two methods. First, the data for each of the eight regions and for each of the two radioactive tracers were analyzed by regression analysis for a total of 16 analyses and Bonferroni's Inequality was applied to prevent false positive results from numerous analyses. By this conservative test, no statistically significant increase in permeation was found for either tracer in any brain region of rats exposed to microwaves. Second, a profile analysis was used to test for a general change in tracer uptake across all brain regions. Using this statistical method, a significant increase in permeation was found for sucrose but not for inulin. A correction factor was then derived from the warm-air experiments to correct for the increase in permeation of the brain associated with change in body temperature. This correction factor was applied to the data for the irradiated animals. After correcting the data for thermal effects of the microwave radiation, no significant increase in permeation was found.

**

Study Type: Nervous System; IN VIVO; RAT
Effect Type: Blood-brain-barrier alterations induced by RFR or heating, as detected by radiotracer techniques
Frequency: 2.45 GHz
Modulation: CW
Power Density: 10, 20, or 30 mW/sq cm
SAR: 2, 4, or 6 W/kg

EXPOSURE CONDITIONS: Anesthetized rats were exposed individually to far-field RFR for 30 min in an anechoic chamber at 22 deg C with their long body axes parallel to the electric field. Other rats were heated for 30 min at 22, 30, or 40 deg C in an oven.

OTHER INFORMATION: Both the left and right femoral vein of the anesthetized rat were surgically exposed, and a mixture of H-3 inulin and C-14 sucrose was injected into the right femoral vein. Five min later, a 0.4-ml blood sample was drawn from the left femoral vein. After another 5 min, each rat was exposed for 30 min at 0, 10, 20, or 30 mW/sq cm at 22 deg C ambient or in an oven at 22, 30, or 40 deg C.

Eight rats were used for each exposure condition. Ten min after such exposure (i.e., 50 min after tracer injection), another 0.4-ml blood sample was drawn by cardiac puncture. The blood samples were processed for liquid scintillation counting and the H-3 and C-14 activities were determined. The serum levels of each tracer at 0, 5, and 50 min were connected with linear segments and the area under the resulting plot was used as an approximation to the integral, I, of the serum concentration over the 50-min period.

Following cardiac puncture, the brain was perfused with saline for 10 min and removed, and 8 samples each of cortex, hypothalamus, cerebellum, hippocampus, striatum, medulla, and midbrain were processed for H-3 and C-14 counting, yielding Tb, the amount of each tracer in each brain region at 50 min. Tracer permeations were expressed as blood-to-brain transfer constants, Ki, defined as the ratio Tb/I. The Ki values of each tracer in each brain region were treated by regression analysis for a total of 16 analyses. To avoid false-positive statistical significance, Bonferroni's Inequality was applied; the $p<0.1$ for significance at the 5% level in a one-sided test was divided by 16, yielding $p=0.006$ as the level for significance.

For positive controls, 9 other rats were injected with hypertonic urea as a bolus into a common carotid artery, in lieu of RFR exposure, and comparisons were made of inulin permeation between ipsilateral and contralateral samples of each brain region. Because only one tracer was used, the level for significance was $p= 0.1/8 =0.013$.

Rectal temperature was measured just before and after the 30-min exposure. Mean rectal temperature changes were linear with oven temperature and power density, with a slope for the latter of 0.09 deg C per mW/sq cm.

For the urea group, significant increases of inulin permeation were obtained in the cortex, striatum, hypothalamus, and hippocampus, indicating that the method used could detect increases in blood-brain-barrier (BBB) permeation. For the rats exposed to RFR, there was no significant ($p<0.006$) permeation of either sucrose or inulin in any of the 8 brain regions. For the oven-heated rats, the only significant permeability increase was of sucrose in the hypothalamus of those exposed at 40 deg C, possibly due to the corresponding core-temperature increase. Under the assumption that equal core-temperature rises produced by RFR- and oven exposure would cause equal BBB changes, corrections based on the 0.09 deg C per mW/sq cm slope cited above and the slopes of Ki-vs-core-temperature plots from the oven data were applied to the RFR permeation results (at 22 deg C), presumably yielding any nonthermal RFR contributions to BBB permeability. Using Bonferroni's Inequality, no significant BBB alterations were seen. These corrections reduced the Ki values by 16% or less and rendered 14 of the 16 p values less significant. A profile analysis was also performed to test for a general change in tracer uptake across all brain regions. The inulin profile was insignificant. The sucrose profile changed significantly with both oven temperature and power density;

however, there was no significant BBB permeation change due to RFR after applying the above corrections.

CRITIQUE: The use of Bonferroni's Inequality to render insignificant some results that were significant at the $p<0.05$ level (false positive results) may be questioned as perhaps too conservative. However, this statistical technique is now widely accepted. To be less conservative, such false positive results could be taken as an indication of a need to repeat those aspects of the experiment with larger sample populations.

The assumption that equivalent BBB changes would be obtained from equal core-temperature rises by RFR- or oven exposure is open to question because the internal distributions of the energy from the two types of source were most likely different, even if the whole-body SARs were about the same. Thus, the corrections based on this assumption, to remove the thermal part of the RFR interaction, are debatable. Nevertheless, if such corrections are taken at face value, the results indicate that there were no significant nonthermal effects of RFR on the BBB. Conversely, in the absence of such corrections, the results indicate the thermal basis of the few significant BBB alterations found. The latter results are consonant with the findings of Merritt et al. (1978) and Sutton and Carroll (1979), who showed that the temperature of the brain must be raised appreciably to alter the permeability of the BBB.

REFERENCES:

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

***

WARD
ELDER
LONG
SVENDSGAARD

/

BBB
CW
IN-VIVO
NERVOUS-SYSTEM
POSITIVE-CONTROL
RAT
RECTAL
RFR
TRACER

//

1982
2450
1
10-30
2-6

///

115
Chang, B.K., A.T. Huang, W.T. Joines, and R.S. Kramer
THE EFFECT OF MICROWAVE RADIATION (1.0 GHZ) ON THE BLOOD-BRAIN BARRIER IN DOGS
Radio Sci., Vol. 17, No. 5S, pp. 165-168 (1982)

*

AUTHOR ABSTRACT: Although a disruptive effect of low-level microwave (MW) radiation on the blood-brain barrier (BBB) of small laboratory animals has been suggested by a number of authors, the relevance of these studies to larger animals has received little attention. Using I-131 albumin as our tracer molecule and cannulation of the cisterna magna and of the femoral vein to permit multiple sampling of cerebrospinal fluid (CSF) and plasma, we have studied the effects of microwave radiation on the BBB in dogs. Measurement of the CSF/plasma distribution ratio (cpm-CSF/cpm-plasma) of I-131 albumin was carried out over a 5-hour period after exposure of the dog's head for 20 minutes to various power densities of continuous wave microwave at a constant frequency of 1.0 GHz. Control animals (n=11) were subjected to the same experiment, but received no MW exposure.

No effect on the BBB was observed in two dogs each at the following power densities: 2, 4, 10, 50, and 200 mW/sq cm. Eleven dogs were exposed to 30 mW/sq cm, and, within this group, there were two animals in which the penetrance of the BBB by the I-131 albumin was increased 4-5 times over controls, and two additional animals which showed twofold to fourfold increased penetrance. However, the CSF:plasma distribution ratios of the remaining animals receiving 30 mW/sq cm did not differ statistically from controls. The results obtained in the four dogs experiencing a postmicrowave alteration of the blood-brain barrier suggest that, for the dog, a microwave "window" effect may be operating very near 30 mW/sq cm.

**

Study Type: Nervous System; IN VIVO; DOG
Effect Type: RFR-induced alterations of the permeability of the blood-brain barrier to albumin radiolabeled with I-131
Frequency: 1.0 GHz
Modulation: CW
Power Density: 2, 4, 10, 30, 50, or 200 mW/sq cm
SAR: Not measured

EXPOSURE CONDITIONS: The heads of anesthetized mongrel dogs on Plexiglas supports were sham-exposed or exposed to RFR in the near field of a horn for 20 min.

OTHER INFORMATION: Prior to exposure, each dog was anesthetized, intubated, and placed on an artificial respirator. A femoral artery and vein were cannulated and a 19-gauge spinal needle was inserted into the cisterna magna. The dog was then injected with I-131-labeled human

serum albumin via the femoral-vein catheter. Following RFR- or sham-exposure, 1-ml samples of venous blood and 0.2-ml samples of cerebrospinal fluid (CSF) were taken simultaneously every 20 min for 5 hr, at the end of which the dogs were in "satisfactory condition." Aliquots of CSF and blood-plasma samples were assayed for radioactivity with a gamma counter, and the results were expressed as ratios of counts per min (CPM) in CSF x 1000 to CPM in plasma as a measure of albumin transfer across the blood-brain barrier (BBB).

Two dogs each were exposed to 2, 4, 10, 50, or 200 mW/sq cm, and 11 dogs were sham-exposed as controls. No significant differences in the CPM-CSF/CPM-plasma ratio (in the units above) were found between RFR-exposed and control dogs at any of these power densities. Two dogs were also exposed at 30 mW/sq cm. One of these exhibited increased albumin penetrance of the BBB, so 9 other dogs were exposed at this power density. Of the latter, 3 showed significantly higher BBB penetrance and the other 6 no significant differences from the controls. The positive results obtained for 4 dogs exposed at 30 mW/sq cm led the investigators to suggest the possible existence of a power density "window" in the vicinity of this value.

The time course of mean CPM-CSF/CPM-plasma ratios over the 5-hr sampling period for the controls (Table 2) was a gradual rise from 0.36 at 20 min (immediately after exposure) to 5.5 at the end of the period, a factor of about 15. For 7 of the dogs exposed at 30 mW/sq cm, the mean value increased from 0.645 at 20 min to 3.43 at 5 hr, a factor of about 5, but the differences from controls at corresponding sampling times were not statistically significant. For 2 of the other dogs exposed at this power density, the mean ratio increased monotonically from 1.44 at 20 min to 17.8 at 5 hr, a factor of about 12. Also, most of the differences from control values at corresponding times were statistically significant. For the remaining 2 dogs exposed at this power density, the ratio was high initially (at 20 min), i.e., 8.1, varied nonmonotonically to a minimum of 6.5 at 80 min and a maximum of 10.35 at 200 min, and decreased to 7.3 at 5 hr. Although the difference in initial mean values relative to controls was significant, the difference in final values was not. However, as seen in Figure 2, the time course for all 11 dogs exposed at 30 mW/sq cm taken as a group, though above the time course for the controls, did not appear to be significantly so, i.e., was within the standard-deviation range for the controls for most of the sampling times.

CRITIQUE: Measurements or estimates of SARs in the dog head might have been useful for comparing these results with those of other investigators (with other species), especially since the power densities were measured in the near field of the horn (with the dog absent, but presumably with the Plexiglas support present, which might have given rise to local alterations of the RFR field at the location of the animal). Also, the presence of the 19-gauge metal needle in the brain during RFR exposure may have affected the SAR in its vicinity.

Open to question is the statistical validity of analyzing separately the results for 4 (in groups of 2) of the 11 dogs exposed at 30 mW/sq cm, particularly since the time course for the group as a whole did not differ significantly from that for the controls. Qualitatively, the time course for the RFR group being above that for the control group may be an indication of an effect. However, even though the dogs were reported as in satisfactory condition at the end of the 5-hr sampling period, it is difficult to believe that the non-RFR aspects of the treatment did not significantly affect the results, especially in view of the observation that the CSF/plasma ratios for the controls increased monotonically during the period. Duplication of the experiment, preferably with refined dosimetry and use of positive controls (i.e., a non-RFR agent known to alter the permeability of the BBB to better establish the validity of the detection methodology), may resolve such questions, particularly the possible existence of a power density window for this effect, which is well above other reported windows, e.g., for Ca++ efflux (Bawin et al., 1975).

REFERENCES:
Bawin, S.M., L.K. Kaczmarek, and W.R. Adey
EFFECTS OF MODULATED VHF FIELDS ON THE CENTRAL NERVOUS SYSTEM
Proc. Nat. Acad. Sci., Vol. 247, pp. 74-81 (1975)

***

CHANG
HUANG
JOINES
KRAMER

/

BBB
CW
DOG
IN-VIVO
NERVOUS-SYSTEM
RFR
TRACER

//

1982
1000
1
2-200
0

///

116
Adey, W.R., S.M. Bawin, and A.F. Lawrence
EFFECTS OF WEAK AMPLITUDE-MODULATED MICROWAVE FIELDS ON CALCIUM EFFLUX FROM AWAKE CAT CEREBRAL CORTEX
Bioelectromagnetics, Vol. 3, No. 3, pp. 295-307 (1982)

*

AUTHOR ABSTRACT: Calcium (Ca-45++) efflux was studied from preloaded cortex in cats immobilized under local anesthesia, and exposed to a 3.0-mW/sq cm 450-MHz field, sinusoidally amplitude modulated at 16 Hz (modulation depth 85%). Tissue dosimetry showed a field of 33 V/m in the interhemispheric fissure (rate of energy deposition 0.29 W/kg). Field exposure lasted 60 min. By comparison with controls, efflux curves from field exposed brains were disrupted by waves of increased Ca45++ efflux. These waves were irregular in amplitude and duration, but many exhibited periods of 20-30 min. They continued into the postexposure period. Binomial probability analysis indicates that the field-exposed efflux curves constitute a different population from controls at a confidence level of 0.96. In about 70% of cases, initiation of field exposure was followed by increased end-tidal CO2 excretion for about 5 min. However, hypercapnea induced by hypoventilation did not elicit increased Ca45++ efflux. Thus this increase with exposure does not appear to arise as a secondary effect of raised cerebral CO2 levels. Radioactivity measurements in cortical samples after superfusion showed Ca45++ penetration at about 1.7 mm/hr, consistent with diffusion of the ion in free solution.

**

Study Type: Nervous System, Mechanisms of Interaction; IN VIVO; CAT
Effect Type: Alterations of calcium binding to cell membranes in the awake cat brain by 16-Hz-amplitude-modulated RFR
Frequency: 450 MHz
Modulation: Sinusoidal amplitude modulation at 16 Hz (modulation depth 85%)
Power Density: 3.0 mW/sq cm Av
SAR: 0.29 W/kg (measured in separate studies)

EXPOSURE CONDITIONS: All exposures were conducted individually in an anechoic chamber, approximately 7 wavelengths long at 450 MHz, maintained at 28 deg C and 30-40% relative humidity. Cats, paralyzed with gallamine triethiodide and placed on artificial respiration, had pressure points and skin incisions from prior surgery infiltrated with a local anesthetic. They were placed in a plastic stereotaxic headholder and oriented at right angles to the incident field, with the exposed cortex of the right cerebral hemisphere nearest to the RF source. Electric field was vertical, and the exposure volume, in the absence of the animal, had a standing-wave ratio of 1.2:1 or less. Field exposure lasted 60 min. Other cats were sham-exposed using identical experimental protocols.

OTHER INFORMATION: Twenty-three female cats weighing between 2.8 and 3.6 kg were used. Data from 19 are presented in Table 2 and Fig. 3 of the report. All animals were prepared surgically under ether anesthesia. The right cerebral cortex was exposed by a trephine hole and a plastic cylindrical well fitted over it, making gentle contact with the pial surface. A physiological medium was added to the well, and all skin incisions and pressure points were infiltrated with local anesthetic. Ether was discontinued, the animal was paralyzed with gallamine triethiodide IV, and artificial respiration was maintained through a tracheotomy. End-tidal CO2 level was monitored and normally maintained at 4%, but was changed during imposed episodes of hypo and hyperventilation. The cat was placed in a stereotaxic headholder for RFR exposure.

Following stabilization of the preparation, the physiological medium in the well bathing the surface of the brain was changed to contain radioactive calcium ion (Ca^{45++}). After a 90-min incubation, this radioactive solution was removed and replaced with 1.0 ml of nonradioactive medium. The solution was completely changed at 10-min intervals throughout the experiment. Samples were taken on removal and assayed for radioactivity by liquid-scintillation-counting techniques.

The field generating system for exposure consisted of a low-frequency waveform generator (16 Hz) amplitude-modulating a phase-lock-loop controlled 450-MHz signal generator. The signal generator output was applied to a linear power amplifier and thence to a standard gain horn. Modulation and harmonic content of the RF signal were periodically measured. Field levels at the animal's location in the exposure chamber were measured both with a Narda probe and an experimental dipole probe provided by the Bureau of Radiological Health. Field levels in tissue were measured in separate studies. Field exposure lasted 60 min and was initiated at different times after completion of incubation of the cortex with Ca^{45++}. Other similarly treated animals were sham-exposed.

The data from these experiments with RFR- and sham-exposed animals were counts, in samples taken at 10-min intervals, of radioactivity resulting from release of radioactive calcium from the previously labeled cortex. The data obtained were consistent with the hypothesis that calcium efflux follows a curve comprising the sum of several exponential terms. A standard linear regression technique was therefore used to develop approximations to the log-transformed data. These fitted lines then represented idealized efflux curves. Deviations from these idealized curves were quantified by calculating the mean of the relative squared deviations between actual data and the fitted data at the sampling points. Next, runs from exposed and sham-exposed animals were selected as pairs. Two pairs of segments were determined on each pair of curves, one pair prior to the RFR exposure, and the second pair from 20 min after onset of exposure to the end of the experiment. (Pairing criteria were rather involved, but were designed to ensure the best matching of the available data.)

Results of the analysis of the means of the relative squared deviations indicated that the total variance in the preexposure epochs was the same for data from RFR- and sham-exposed animals. By contrast, the totals of variance in the samples from RFR-exposed cortex showed an increase for the second epoch as compared with corresponding sham-exposed cortex. A 1-tailed binomial probability test was used to show that this increase in variance was significant at the $p<0.05$ level. Subsequent experiments showed that the effect was not a consequence of alteration of end-tidal CO2 levels, i.e., not secondary to raised cerebral CO2 levels.

CRITIQUE: This paper is the first to report alterations in the normal pattern of Ca45++ efflux in the brains of intact subjects following exposure to modulated RFR. The cortical well superfusion technique used in this study was developed in the senior author's laboratory over the last 10 years. As reported, many steps and checks were taken to prevent artifact from leakage of the physiological test medium, or from leakage of blood or cerebrospinal fluid. Similar care was taken in the exposure of the subjects.

The description of the data analysis methods is somewhat unclear on several points. Although there is repeated reference to the mean of the relative squared deviation (MRSD), the actual expression given in the text for this quantity is the relative squared deviation itself, because it is not divided by the number of data points, N, to form the mean. This appears also in Table 2. Recalculation of the values of Table 2 by dividing them by their respective Ni yields new values that do not, however, alter the results of the binomial test when applied to the new data.

The data-analysis section also makes no reference to the actual fitted values for the RFR- and sham-exposed animals. All curves, for RFR- and sham-exposed, are approximated by straight lines over the two (log-transformed) segments. No results are given for these fitted values. It would be of interest to know whether these fitted curves showed statistically significant differences for RFR- and sham-exposed cases. The absence of this information seems to imply that the only difference between the RFR- and sham-exposed calcium efflux curves was in the oscillations about the idealized straight-line fit to the data, and not between the straight-line values themselves.

Unlike other studies by these authors (Bawin and Adey, 1976), only the one modulation frequency was used in the present study. Whether CW or other modulation frequencies are also effective in causing fluctuations of Ca45++ efflux about the exponential decay curve postexposure remains unresolved. Likewise, the significance of these differences between RFR- and sham-exposed cases with respect to human health awaits further resolution.

REFERENCES:
Bawin, S.M. and W.R. Adey
SENSITIVITY OF CALCIUM BINDING IN CEREBRAL TISSUE TO WEAK ENVIRONMENTAL FIELDS OSCILLATING AT LOW FREQUENCY
Proc. Nat. Acad. Sci., Vol. 73, No. 6, pp. 1999-2003 (1976)

***

ADEY
BAWIN
LAWRENCE

/

CALCIUM
CAT
EFFLUX
IN-VIVO
MECHANISMS
MODULATED
NERVOUS-SYSTEM
RFR

//

1982
450
1
3.0
0.29

///

117
Schrot, J., J.R. Thomas, and R.A. Banvard
MODIFICATION OF THE REPEATED ACQUISITION OF RESPONSE SEQUENCES IN RATS BY LOW-LEVEL MICROWAVE EXPOSURE
Bioelectromagnetics, Vol. 1, No. 1, pp. 89-99 (1980)

*

AUTHOR ABSTRACT: The acute effects of microwave exposure on a repeated acquisition baseline were investigated in three rats. Each session the animals acquired a different four-member response sequence. Each of the first three correct responses advanced the sequence to the next member, and the fourth correct response produced food reinforcement. Incorrect responses produced a three-second timeout. Baseline and control sessions were characterized by a decrease in errors within each session. The animals were acutely exposed to a 2.8 GHz pulsed-microwave field prior to test sessions, with average power densities ranging from 0.25 to 10 mW/sq cm. In comparison to control sessions, 1/2 hour of exposure to microwave radiation at power densities of 5 and 10 mW/sq cm increased errors and altered the pattern of within-session acquisition. Exposure to the 10 mW/sq cm power density decreased the rate of sequence completion in all animals. The results of exposures at 0.25, 0.5, and 1 mW/sq cm power densities were generally within the control range. The results are interpreted as indicating a disruption in the discriminative stimulus control of the repeated acquisition behavior.

**

Study Type: Behavior; IN VIVO; RAT
Effect Type: Alteration of the rate of completion of a four-member behavioral response sequence producing food reinforcement in rats exposed to RFR prior to testing
Frequency: 2.8 GHz
Modulation: 2-microsecond pulses at 500 pps
Power Density: 0.25, 0.5, 1, 5, and 10 mW/sq cm Av at 0.001 duty cycle
SAR: 0.7 W/kg at 5 mW/sq cm, 1.7 W/kg at 10 mW/sq cm (mean values calculated from core-temperature rises in rats exposed in restraint harnesses)

EXPOSURE CONDITIONS: Immediately before behavior assessment, animals were exposed (or sham-exposed) for 30 min at one of the 5 power densities in a microwave anechoic chamber at 21 deg C. They were restrained in a sleeve holder constructed of fine plastic mesh suspended from a styrofoam frame located 68 cm (approximately 6.3 wavelengths) in front of a standard-gain horn. Electric field polarization was vertical. Animals were exposed laterally with the H-vector parallel to the long body dimension. Incident power densities were measured with a Narda 8315A monitor and 8321 probe. Air flow was 3.05 m/min at the subject's normal exposure position.

OTHER INFORMATION: The study was designed to investigate the effects on the acquisition of behavior of RFR at average levels equal to or below 10 mW/sq cm. Rats were trained to acquire a different four-member chain of responses each session. They were maintained by food reinforcement and subsequently exposed to RFR for assessment of behavioral effects.

Three male albino rats were used. They were approximately 120 days old at the start of the study, weighing 275 g, and were maintained at approximately 80% of their free-feeding weights. They were housed individually in home cages and provided with water ad libitum.

The testing apparatus comprised a standard 2-lever rat chamber modified to include a third lever. The chamber was enclosed in a ventilated sound-attenuating enclosure. Each rat was trained to respond on each of the 3 levers individually, and responses were reinforced with 45-mg food pellets. Each rat then proceeded through a sequence of increasing chain lengths (i.e., responding on 2, 3, or 4 levers in sequence) incorporating auditory stimuli until the predetermined 4-lever sequence was reached. The rats were thus required to perform 4 lever presses (1 lever repeating), such as left (L), center (C), left (L), right (R), i.e., LCLR, or other combinations, with 4 auditory signals (900-Hz tone, 1-per-second clicks, 2000-Hz tone, and 10-per-second clicks) indicating the need for the next lever response in the chain.

The auditory stimuli were set at 72 dB, measured in the cage, and their ordering was the same from session to session. The ordering of lever responses was changed randomly from session to session. Correct lever responses to the auditory stimuli advanced the chain to the next member and ultimately produced food pellet reinforcement. Incorrect responses produced a 3-second timeout, signaled by turning off the houselight and current auditory stimulus and turning on a 2.8-Hz, 92-dB auditory stimulus. Incorrect responses did not reset the sequence. Each auditory stimulus was presented until a correct response advanced the sequence to the next member of the chain, thereby producing the next auditory stimulus. Sessions were conducted at daily scheduled times, 5 days a week, and were terminated after 150 reinforcements or 2 hr, whichever occurred first. Each of the 3 rats was therefore tested once or twice a week.

Baseline response training took 4 months. Following 7 sessions of adaptation to the sleeve holder, a series of RFR exposures was carried out. Animals were exposed to RFR for 30 min immediately prior to behavioral testing on 1 or 2 days a week. Each animal was exposed to 0.25, 0.5, 1, 5, and 10 mW/sq cm average power density, with exposures conducted in mixed order and each level presented a minimum of 3 times (a total of at least 15 actual exposure sessions for each rat). Sham irradiations were conducted throughout the exposure series. A normal baseline session always followed both sham- and RFR-exposure sessions.

For the 3 rats, a 30-min presession exposure at 10 mW/sq cm resulted in increased error responding, decreased sequence-completion rates, and alteration in the normal pattern of acquisition. These changes were termed by the authors as "disruption of the daily acquisition curve generated by the repeated-acquisition procedure". Similar effects, but to a lesser extent, were seen at 5 mW/sq cm. For exposures below 5 mW/sq cm, the majority of the data points fell within the control range, but a few were outside it. The significance of these few points is uncertain. Observation of animals during a session revealed that increase in error responding was frequently associated with failure of the animal to switch response locations after a single lever press, which could be interpreted as a loss of stimulus control by the animal.

CRITIQUE: This study was carried out by investigators familiar with the myriad problems associated with both long-term repeated RFR exposure of subjects and the difficulties of long-term testing of a complex behavioral task. As is the case with such tests, the present study of necessity was confined to only a small number of rats (3) because of the long time required for stable baseline acquisition of the complex learning tasks. Similar RFR-induced disruption of stimulus control in the context of multiple schedules of reinforcement was demonstrated by Thomas et al. (1975) and Mitchell et al. (1977). The mechanism of action of RFR in the present study is not clear. At 5 and 10 mW/sq cm average power densities, the peak power densities were 5 and 10 W/sq cm, respectively. Together with the 2-microsecond pulse width, these peak levels were sufficient to cause RFR-auditory responses. Likewise, selective brain heating arising from localized high SAR values might have been involved. As the authors indicate, however, "any explanation will require effects that persist for 60 to 90 min postexposure". Such mechanisms for the present effect have not been determined here. However, the fact remains that there are clear-cut and definite alterations in the performance of this complex behavioral task at 10 mW/sq cm , and to a lesser extent at 5 mW/sq cm. The sensitivity of this test with regard to other environmental agents or stimuli was not tested, nor is it discussed. Therefore, the significance of such behavioral alterations in terms of human health and safety is presently unresolved.

REFERENCES:

Thomas, J.R., E.C. Finch, D.W. Fulk, and L.S. Burch
EFFECTS OF LOW-LEVEL MICROWAVE RADIATION ON BEHAVIORAL BASELINES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 425-432 (1975)

Mitchell, D.S., W.G. Switzer, and E.L. Bronaugh
HYPERACTIVITY AND DISRUPTION OF OPERANT BEHAVIOR IN RATS AFTER MULTIPLE EXPOSURES TO MICROWAVE RADIATION
Radio Sci., Vol. 12, No. 6S, pp. 263-271 (1977)

***

[illegible]
[illegible]
[illegible]

[illegible]
[illegible]
[illegible]
KAI
REPEA[illegible]
RFR

/

1980
2800
0.001
0.25-10
0.035-1.7

///

118
Takashima, S., B. Onaral, and H.P. Schwan
EFFECTS OF MODULATED RF ENERGY ON THE EEG OF MAMMALIAN BRAINS
Rad. and Environm. Biophys., Vol. 16, pp. 15-27 (1979)

*

AUTHOR ABSTRACT: The effects of modulated radio frequency fields on mammalian EEGs were investigated using acute and chronic irradiations at non-thermal level. The EEG signals were computer processed to obtain power spectra. Rabbits were exposed to the field for 2 h a day for 6 weeks at 1-10 MHz (15 Hz modulation) at the level of 0.5-1 kV/M. Silver electrodes placed on the skull surface were used for recording of the EEG. Usually they were removed immediately after initial recordings of the EEG and reinserted before the final and intermediate EEG recordings. With this arrangement, modulated RF fields produced a change in EEG patterns by enhancing the low frequency components and decreasing high frequency activities. On the other hand, acute irradiations did not produce noticeable changes in the EEG at the level of 0.5-1 kV/M (1-30 MHz, 60 Hz modulation) as long as the use of intracranial electrodes was avoided.

**

Study Type: Nervous System; IN VIVO; RABBIT
Effect Type: Changes in EEG patterns
Frequency: 1-30 MHz
Modulation: 15 or 60 Hz
Power Density: 500-1000 V/m (near-field electric-field intensity), (66-270 mW/sq cm free-space equivalent)
SAR: Not stated

EXPOSURE CONDITIONS: Near-field exposures were conducted between two 30 X 30 cm square aluminum plates spaced 20 cm. Electric field strengths ranged from 500 V/m to 1 kV/m. Acute exposures were for 2-3 hr to 1-10 MHz modulated at 60 Hz, with the animals anesthetized. Chronic exposures were 2 hr/day for 6 weeks to 1.2 MHz modulated at 15 Hz, without anesthesia.

OTHER INFORMATION: Male rabbits, 4-5 months old, weight 2-3 kg, were used in all experiments.

EEG signals were amplified with a preamplifier having a pass band of 3-100 Hz and a 60-Hz notch filter. In initial experiments, it was found that unprocessed time-domain EEG signals were difficult to interpret. Consequently, EEG time-domain signals were sampled at 5-ms intervals (1024 points), digitized, transformed to frequency-domain complex spectra, and thence to power spectra using the fast-Fourier-transform (FFT) technique. Smoothing of power spectra was performed by applying Hann's function to autocorrelograms (Fourier transforms of power spectra), which were Fourier transformed again to obtain smoothed power spectra. Sequential displays of smoothed power spectra (usually 17

spectra at 3-min intervals) were examined to detect time-invariant features.

Typical power-spectra sequences from anesthetized rabbits before RFR exposure showed frequency components between 5 and 15 Hz that varied during each sequence, indicating the absence of a dominant component. These EEGs were denoted as "normal" by the investigators.

In one set of preliminary experiments (5 animals) involving acute exposure to 60-Hz-modulated RFR, stainless-steel electrodes chronically implanted in the brain were allowed to remain in the cranial cavity during irradiation. The sequential set of power spectra obtained after RFR exposure showed a clustering of amplitude peaks in the range 2-5 Hz, which persisted over the postexposure recording period (40-60 min). Reduction of high-frequency components was also noted. In a second set of experiments (2 animals), the EEG electrodes were removed prior to RFR exposure and reinserted after exposure. The power spectra obtained from the latter experiments resembled normal EEGs as defined above; no clustering of spectral components was apparent. Therefore, the EEG alterations in the first set of experiments were attributed by the investigators to the local field created by the presence of metal electrodes in the cranial cavity.

To investigate the effects of chronic exposure, 4 unanesthetized animals were exposed 2 hr/day to 1.2-MHz RFR modulated at 15 Hz for 6 weeks. EEGs were recorded using silver electrodes placed directly on the skull before and after periods of irradiation. EEGs were monitored every 2 weeks. A sequential display of power spectra taken after 4 weeks of exposure showed an ordering of low-frequency spectral peaks and reduction of high-frequency components similar to the acute-exposure data taken with intracranial electrodes. The abnormal patterns began to appear after 2-3 weeks of exposure. The investigators constructed histograms from power-spectrum sequences derived from 4-week exposures and normal EEGs. The histogram for the RFR-exposed animals showed major peaks at 2 and 10 Hz, whereas the major peaks for the normal EEGs were at 4.5, 8, and 11.5 Hz.

Assuming that the rabbit head (without intracranial metal electrodes) could be modeled as a homogeneous conducting sphere immersed in a 10-MHz field of 500 V/m, the investigators calculated that the current density within the head was 0.082 mA/sq cm. Consequently, they characterized the above positive result from the chronic study as a nonthermal RFR effect.

CRITIQUE: Adequate dosimetry data were not presented, notably measurements or estimates of SARs in the head, so it is questionable to characterize any positive findings as thermal or nonthermal. Also, in their acute-exposure experiments, it is not clear why 60 Hz was used as the modulation frequency, especially since the EEG signals were passed through a 60-Hz notch filter.

In contrast with previous work by this group (Kritikos et al., 1975), the use of metal electrodes during RFR exposure was shown to yield

artifactual EEG changes. [The problems of recording EEGs under such conditions are treated extensively in National Council on Radiation Protection (NCRP) report, 1981. Such problems include field distortion, field enhancement in the vicinity of such electrodes, and possible tissue damage.]

In the chronic-exposure experiments (with 15-Hz-modulated RFR), although the electrodes were not present during the RFR exposures, there is confusion in the description of electrode placement before and after exposure. In the text, attachment to the "skull" was described, whereas in Table 1, "scalp" was used to describe the electrode arrangement. It is not clear whether surgery was involved.

The rabbits apparently were used as their own control group in that data were compared with "normal" (preexposure) data from the same group. However, the absence of a similarly treated but sham-exposed group makes it difficult to assess whether the reported changes were the result of RFR exposure per se, or perhaps of adaptation to the repeated exposure procedures, such as handling and recording.

When the power spectra for EEGs taken at short time intervals (3 min) in a sequence are highly variable among one another, it is difficult to quantitatively assess differences among sequences. Autoregressive spectral estimation techniques (Kay et al., 1981) are perhaps more appropriate for analysis of EEG data than FFT techniques, since interval definition is problematic for nonstationary data. (Takashima et al. did not discuss the choice of truncation interval in their FFT analyses.) Qualitatively, nevertheless, their results for the chronic-exposure experiments appear to show enhancement of low-frequency power-spectral components and reduction of high-frequency activities. However, comparison of data from the anesthetized animals used in the acute experiments with data from the unanesthetized animals used in the chronic experiments lacks analysis of the effects of anesthesia as a possible confounding factor. Also, it is not clear why only the data taken after 4 weeks of exposure (and not those after 2- and 6 weeks) were presented.

The chronic-exposure results of the authors differed from those of Chou et al. (1982), who exposed 6 rabbits 2 hr/day for 3 months to 2.45-GHz-CW RFR and 6 rabbits to 2.45-GHz-pulsed RFR at 1.5 mW/sq cm average power density. Six other rabbits were similarly sham-exposed. Chronically implanted carbon-loaded Teflon electrodes were used to record EEGs weekly during exposure. No significant differences in EEG were found among the 3 groups.

REFERENCES:

Chou, C.-K., A.W. Guy, J.B. McDougall, and L.-F. Han
EFFECTS OF CONTINUOUS AND PULSED CHRONIC MICROWAVE EXPOSURE ON RABBITS
Radio Sci., Vol. 17, No. 5S, pp. 185-193 (1982)

Kay, S.M. and S.L. Marple
SPECTRUM ANALYSIS--A MODERN PERSPECTIVE
Proc. IEEE, Vol. 69, No. 11, pp. 1380-1419 (1981)

Kritikos, H., S. Takashima, and H.P. Schwan
EFFECTS OF RF FIELDS ON NERVOUS ACTIVITIES
Microwave Power Symp. 1975 Proc., Ontario, Canada, pp. 64-65 (1975)

NCRP--National Council on Radiation Protection and Measurements
RADIOFREQUENCY ELECTROMAGNETIC FIELDS: PROPERTIES, QUANTITIES AND UNITS, BIOPHYSICAL INTERACTION, AND MEASUREMENTS
NCRP Report No. 67, Washington, D.C., pp. 78-80, 108-111 (1981)

***

TAKASHIMA
ONARAL
SCHWAN

/

BIORHYTHM
EEG
IN-VIVO
MODULATED
NERVOUS-SYSTEM
RABBIT
RFR

//

1979
1-30
I
66-270
0

///

APPENDIX B

MASTER LIST OF ANALYSES

PRECEDING PAGE BLANK-NOT FILMED

MASTER LIST OF ANALYSES

62
Adair, E.R. and B.W. Adams
MICROWAVES MODIFY THERMOREGULATORY BEHAVIOR IN SQUIRREL MONKEY
Bioelectromagnetics, Vol. 1, No. 1, pp. 1-20 (1980) (II-72)

116
Adey, W.R., S.M. Bawin, and A.F. Lawrence
EFFECTS OF WEAK AMPLITUDE-MODULATED MICROWAVE FIELDS ON CALCIUM EFFLUX FROM AWAKE CAT CEREBRAL CORTEX
Bioelectromagnetics, Vol. 3, No. 3, pp. 295-307 (1982) (III-152)

32
Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979) (I-104)

111
Albert, E.N. and J.M. Kerns
REVERSIBLE MICROWAVE EFFECTS ON THE BLOOD-BRAIN BARRIER
Brain Res., Vol. 230, Nos. 1-2, pp. 153-164 (1981) (III-134)

19
Appleton, B., S. Hirsh, R.O. Kinion, M. Soles, G.C. McCrossan, and R.M. Neidlinger,
MICROWAVE LENS EFFECTS IN HUMANS
Arch. Ophthalmol., Vol. 93, pp. 257-258 (1975) (I-72)

39
Bawin, S.M. and W.R. Adey
SENSITIVITY OF CALCIUM BINDING IN CEREBRAL TISSUE TO WEAK ENVIRONMENTAL FIELDS OSCILLATING AT LOW FREQUENCY
Proc. Nat. Acad. Sci., Vol. 73, No. 6, pp. 1999-2003 (1976) (I-124)

40
Bawin, S.M., L.K. Kaczmarek, and W.R. Adey
EFFECTS OF MODULATED VHF FIELDS ON THE CENTRAL NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 74-81 (1975) (I-127)

84
Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981) (III-25)

81
Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982) (III-13)

PRECEDING PAGE BLANK-NOT FILMED

50
Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978) (II-24)

90
Bielski, J., A. Sawinska, and J. Pianowska
BIOELECTRICAL BRAIN ACTIVITY IN EMPLOYEES EXPOSED TO VARIOUS FREQUENCIES OF ELECTROMAGNETIC FIELDS
Proc. URSI, Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 193-195 (June-July 1980) (III-46)

41
Blackman, C.F., J.A. Elder, C.M. Weil, S.G. Benane, D.C. Eichinger, and D.E. House
INDUCTION OF CALCIUM-ION EFFLUX FROM BRAIN TISSUE BY RADIO-FREQUENCY RADIATION: EFFECTS OF MODULATION FREQUENCY AND FIELD STRENGTH
Radio Sci., Vol. 14, No. 6S, pp. 93-98 (1979) (I-130)

13
Blackman, C.F., M.C. Surles, and S.G. Benane
THE EFFECT OF MICROWAVE EXPOSURE ON BACTERIA: MUTATION INDUCTION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 406-413 (1976) (I-56)

1
Burdeshaw, J.A. and S. Schaffer
FACTORS ASSOCIATED WITH THE INCIDENCE OF CONGENITAL ANOMALIES: A LOCALIZED INVESTIGATION
Final Report, Report No. XXIII, 24 May 1973-31 March 1976, Contract No. 68-02-0791, EPA 600/1-77-016 (March 1977) (I-24)

24
Cain, C.A. and W.J. Rissman
MAMMALIAN AUDITORY RESPONSES TO 3.0 GHz MICROWAVE PULSES
IEEE Trans. Biomed. Eng., Vol. 25, No. 3, pp. 288-293 (1978) (I-86)

51
Carpenter, R.L. and E.M. Livstone
EVIDENCE FOR NONTHERMAL EFFECTS OF MICROWAVE RADIATION: ABNORMAL DEVELOPMENT OF IRRADIATED INSECT PUPAE
IEEE Trans. Microwave Theory and Tech., Vol. 19, No. 2, pp. 173-178 (1971) (II-27)

115
Chang, B.K., A.T. Huang, W.T. Joines, and R.S. Kramer
THE EFFECT OF MICROWAVE RADIATION (1.0 GHZ) ON THE BLOOD-BRAIN BARRIER IN DOGS
Radio Sci., Vol. 17, No. 5S, pp. 165-168 (1982) (III-149)

52
Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977) (II-31)

53
Chernovetz, M.E., D.R. Justesen, N.W. King, and J.E. Wagner
TERATOLOGY, SURVIVAL, AND REVERSAL LEARNING AFTER FETAL IRRADIATION OF MICE BY 2450-MHZ MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 391-409 (1975) (II-35)

25
Chou, C.-K. and R. Galambos
MIDDLE-EAR STRUCTURES CONTRIBUTE LITTLE TO AUDITORY PERCEPTION OF MICROWAVES
J. Microwave Power, Vol. 14, No. 4, pp. 321-326 (1979) (I-88)

26
Chou, C.-K., and A.W. Guy
MICROWAVE-INDUCED AUDITORY RESPONSES IN GUINEA PIGS: RELATIONSHIP OF THRESHOLD AND MICROWAVE-PULSE DURATION
Radio Sci., Vol. 14, No. 6S, pp. 193-197 (1979) (I-90)

27
Chou, C.-K., A.W. Guy, and R. Galambos
CHARACTERISTICS OF MICROWAVE-INDUCED COCHLEAR MICROPHONICS
Radio Sci., Vol. 12, No. 6S, pp. 221-227 (1977) (I-92)

43
Chou, C.-K., A.W. Guy, J.B. McDougall, and L.-F. Han
EFFECTS OF CONTINUOUS AND PULSED CHRONIC MICROWAVE EXPOSURE ON RABBITS
Radio Sci., Vol. 17, No. 5S, pp. 185-193 (1982) (I-138)

20
Cleary, S.F. and B.S. Pasternack
LENTICULAR CHANGES IN MICROWAVE WORKERS--A STATISTICAL STUDY
Arch. Environ. Health, Vol. 12, pp. 23-29 (1966) (I-74)

21
Cleary, S.F., B.S. Pasternack, and G.W. Beebe
CATARACT INCIDENCE IN RADAR WORKERS
Arch. Environ. Health, Vol. 11, pp. 179-182 (1965) (I-76)

2
Cohen, B.H., A.M. Lilienfeld, S. Kramer, and L.C. Hyman
PARENTAL FACTORS IN DOWN'S SYNDROME-RESULTS OF THE SECOND BALTIMORE CASE-CONTROL STUDY
In E.G. Hook and I.H. Porter (eds.), POPULATION GENETICS-STUDIES IN HUMANS, Academic Press, New York, pp. 301-352 (1977) (I-27)

71
Czerski, P.
MICROWAVE EFFECTS ON THE BLOOD-FORMING SYSTEM WITH PARTICULAR REFERENCE TO THE LYMPHOCYTE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 232-242 (1975) (II-102)

80
Dardalhon, M., D. Averbeck, and A.J. Berteaud
DETERMINATION OF A THERMAL EQUIVALENT OF MILLIMETER MICROWAVES IN LIVING CELLS
J. Microwave Power, Vol. 14, No. 4, pp. 307-312 (1979) (II-134)

54
Dietzel, F.
EFFECTS OF ELECTROMAGNETIC RADIATION ON IMPLANTATION AND INTRAUTERINE DEVELOPMENT OF THE RAT
Ann. N.Y. Acad. Sci., Vol. 247, pp. 367-376 (1975) (II-39)

14
Dutta, S.K., W.H. Nelson, C.F. Blackman, and D.J. Brusick
LACK OF MICROBIAL GENETIC RESPONSE TO 2.45-GHZ CW AND 8.5- TO 9.6-GHZ PULSED MICROWAVES
J. Microwave Power, Vol. 14, No. 3, pp. 275-280 (1979) (I-58)

88
Fisher, P., J.K. Lauber, and W.A.G. Voss
THE EFFECT OF LOW-LEVEL 2450 MHZ CW MICROWAVE IRRADIATION AND BODY TEMPERATURE ON EARLY EMBRYONAL DEVELOPMENT IN CHICKENS
Radio Sci., Vol. 14, No. 6S, pp. 159-163 (1979) (III-38)

28
Foster, K.R. and E.D. Finch
MICROWAVE HEARING: EVIDENCE FOR THERMOACOUSTIC AUDITORY STIMULATION BY PULSED MICROWAVES
Science, Vol. 185, pp. 256-258, 19 July 1974 (I-94)

29
Frey, A.H. and E. Coren
HOLOGRAPHIC ASSESSMENT OF A HYPOTHESIZED MICROWAVE HEARING MECHANISM
Science, Vol. 206, pp. 232-234, 12 Oct 1979 (I-96)

33
Frey, A.H., S.R. Feld, and B. Frey
NEURAL FUNCTION AND BEHAVIOR: DEFINING THE RELATIONSHIP
Ann. N.Y. Acad. Sci., Vol. 247, pp. 433-439 (1975) (I-106)

30
Frey, A.H. and R. Messenger, Jr.
HUMAN PERCEPTION OF ILLUMINATION WITH PULSED ULTRAHIGH-FREQUENCY ELECTROMAGNETIC ENERGY
Science, Vol. 181, pp. 356-358, 27 July 1973 (I-98)

87
Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980) (III-35)

99
Galvin, M.J., D.I. McRee, C.A. Hall, J.P. Thaxton, and C.R. Parkhurst
HUMORAL AND CELL-MEDIATED IMMUNE FUNCTION IN ADULT JAPANESE QUAIL FOLLOWING EXPOSURE TO 2.45-GHZ MICROWAVE RADIATION DURING EMBRYOGENY
Bioelectromagnetics, Vol. 2, No. 3, pp. 269-278 (1981) (III-81)

100
Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b) (III-86)

22
Guy, A.W., J.C. Lin, P.O. Kramar, and A.F. Emery
EFFECT OF 2450-MHz RADIATION ON THE RABBIT EYE
IEEE Trans. Microwave Theory and Techniques, Vol. 23, No. 6, pp. 492-498 (1975) (I-78)

44
Hagmann, M.J. and O.P. Gandhi
NUMERICAL CALCULATION OF ELECTROMAGNETIC ENERGY DEPOSITION IN MODELS OF MAN WITH GROUNDING AND REFLECTOR EFFECTS
Radio Sci., Vol. 14, No. 6S, pp. 23-29 (1979) (I-150)

45
Hagmann, M.J., O.P. Gandhi, and C.H. Durney
NUMERICAL CALCULATION OF ELECTROMAGNETIC ENERGY DEPOSITION FOR A REALISTIC MODEL OF MAN
IEEE Trans. Microwave Theory and Tech., Vol. 27, No. 9, pp. 804-809 (1979) (I-152)

46
Hagmann, M.J., O.P. Gandhi, J.A. D'Andrea, and I. Chatterjee
HEAD RESONANCE: NUMERICAL SOLUTION AND EXPERIMENTAL RESULTS
IEEE Trans. Microwave Theory and Tech., Vol. 27, No. 9, pp. 809-813 (1979) (I-154)

15
Hamnerius, Y., H. Olofsson, A. Rasmuson, and B. Rasmuson
A NEGATIVE TEST FOR MUTAGENIC ACTION OF MICROWAVE RADIATION IN DROSOPHILA MELANOGASTER
Mutation Res., Vol. 68, No. 2, pp. 217-223 (1979) (I-60)

72
Hamrick, P.E., D.I. McRee, P. Thaxton, and C.R. Parkhurst
HUMORAL IMMUNITY OF JAPANESE QUAIL SUBJECTED TO MICROWAVE RADIATION DURING EMBRYOGENY
Health Phys., Vol. 33, pp. 23-33 (1977) (II-105)

73
Huang, A.T. and N.G. Mold
IMMUNOLOGIC AND HEMATOPOIETIC ALTERATIONS BY 2.450-MHZ ELECTROMAGNETIC RADIATION
Bioelectromagnetics, Vol. 1, No. 1, pp. 77-87 (1980) (II-108)

74
Huang, A.T., M.E. Engle, J.A. Elder, J.B. Kinn, and T.R. Ward
THE EFFECT OF MICROWAVE RADIATION (2450 MHZ) ON THE MORPHOLOGY AND CHROMOSOMES OF LYMPHOCYTES
Radio Sci., Vol. 12, No. 6S, pp. 173-177 (1977) (II-111)

85
Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982) (III-28)

83
Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a) (III-21)

82
Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915 MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b) (III-17)

3
Kalyada, T.V., P.P. Fukalova, and N.N. Goncharova
BIOLOGIC EFFECTS OF RADIATION IN THE 30-300 MHZ RANGE
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 52-57 (1974) (I-30)

4
Klimkova-Deutschova, E.
NEUROLOGIC FINDINGS IN PERSONS EXPOSED TO MICROWAVES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 268-272 (1974) (I-32)

47
Kritikos, H.N. and H.P. Schwan
FORMATION OF HOT SPOTS IN MULTILAYER SPHERES
IEEE Trans. Biomed. Eng., Vol. 22, pp. 168-172 (1976) (I-157)

48
Kritikos, H.N. and H.P. Schwan
THE DISTRIBUTION OF HEATING POTENTIAL INSIDE LOSSY SPHERES
IEEE Trans. Biomed. Eng., Vol. 22, No. 6, pp. 457-463 (1975) (I-159)

66
Lancranjan, I., M. Maicanescu, E. Rafaila, I. Klepsch, and H.I. Popescu
GONADIC FUNCTION IN WORKMEN WITH LONG-TERM EXPOSURE TO MICROWAVES
Health Phys., Vol. 29, pp. 381-383 (1975) (II-84)

89
Lester, J.R. and D.F. Moore
CANCER MORTALITY AND AIR FORCE BASES
J. Bioelectricity, Vol. 1, No. 1, pp. 77-82 (1982a) (III-41)

91
Lester, J.R. and D.F. Moore
CANCER INCIDENCE AND ELECTROMAGNETIC RADIATION
J. Bioelectricity, Vol. 1, No. 1, pp. 59-76 (1982b) (III-49)

105
Liburdy, R.P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977) (III-108)

103
Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHYOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979) (III-99)

102
Liburdy. R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980) (III-95)

97
Liddle, C.G., J.P. Putnam, J.S. Ali, J.Y. Lewis, B. Bell, M.W. West, and O.H. Lewter
ALTERATION OF CIRCULATING ANTIBODY RESPONSE OF MICE EXPOSED TO 9-GHZ PULSED MICROWAVES
Bioelectromagnetics, Vol. 1, No. 4, pp. 397-404 (1980) (III-72)

5
Lilienfeld, A.M., J. Tonascia, S. Tonascia, C.H. Libauer, G.M. Cauthen, J.A. Markowitz, and S. Weida
FOREIGN SERVICE HEALTH STATUS STUDY: EVALUATION OF STATUS OF FOREIGN SERVICE AND OTHER EMPLOYEES FROM SELECTED EASTERN EUROPEAN POSTS
Final Report, July 31, 1978, Contract No. 6025-619073, Dept. of Epidemiology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD (1978) (I-35)

109
Lin, J.C. and M.F. Lin
STUDIES ON MICROWAVE AND BLOOD-BRAIN BARRIER INTERACTION
Bioelectromagnetics, Vol. 1, No. 3, pp. 313-323 (1980) (III-126)

113
Lin, J.C. and M.F. Lin
MICROWAVE HYPERTHERMIA-INDUCED BLOOD-BRAIN BARRIER ALTERATIONS
Radiat. Res., Vol. 89, pp. 77-87 (1982) (III-141)

79
Lin, J.C., J.C. Nelson, and M.E. Ekstrom
EFFECTS OF REPEATED EXPOSURE TO 148-MHZ RADIO WAVES ON GROWTH AND HEMATOLOGY OF MICE
Radio Sci., Vol. 14, No. 6S, pp. 173-179 (1979) (II-130)

55
Lindauer, G.A., L.M. Liu, G.W. Skewes, and F.J. Rosenbaum
FURTHER EXPERIMENTS SEEKING EVIDENCE OF NONTHERMAL BIOLOGICAL EFFECTS MICROWAVE RADIATION
IEEE Trans. Microwave Theory and Tech., Vol. 22, No. 8, pp. 790-793 (1974) (II-41)

56
Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE RELATION OF TERATOGENESIS IN TENEBRIO MOLITOR TO THE INCIDENCE OF LOW-LEVEL MICROWAVES
IEEE Trans. Microwave Theory and Tech., Vol. 23, No. 11, pp. 929-931 (1975) (II-44)

67
Lotz, W.G. and S.M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHIPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respirat. Environ. Exercise Physiol., Vol. 44, No. 3, pp. 438-445 (1978) (II-87)

68
Lu, S.-T., N. Lebda, S.M. Michaelson, S. Pettit, and D. Rivera
THERMAL AND ENDOCRINOLOGICAL EFFECTS OF PROTRACTED IRRADIATION OF RATS BY 2450-MHZ MICROWAVES
Radio Sci., Vol. 12, No. 6S, pp. 147-156 (1977) (II-90)

69
Magin, R.L., S.-T. Lu, and S.M. Michaelson
MICROWAVE HEATING EFFECT ON THE DOG THYROID GLAND
IEEE Trans. Biomed. Eng., Vol. 24, No. 6, pp. 522-529 (1977a) (II-93)

70
Magin, R.L., S.-T. Lu, and S.M. Michaelson
STIMULATION OF DOG THYROID BY LOCAL APPLICATION OF HIGH INTENSITY MICROWAVES
Am. J. Physiol., Vol. 233, No. 5, pp. E363-E368 (1977b) (II-96)

23
McAfee, R.D., A. Longacre, Jr., R.R. Bishop., S.T. Elder, J.G. May, M.G. Holland, and R. Gordon
ABSENCE OF OCULAR PATHOLOGY AFTER REPEATED EXPOSURE OF UNANESTHETIZED MONKEYS TO 9.3-GHZ MICROWAVES
J. Microwave Power, Vol. 14, No. 1, pp. 41-44 (1979) (I-80)

98
McRee, D.I., R. Faith, E.E. McConnell, and A.W. Guy
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: EVALUATION OF HEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 45-52 (1980) (III-76)

57
McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977) (II-47)

34
Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environ. Biophys., Vol.15, pp. 367-377 (1978) (I-109)

92
Milham, S., Jr.
MORTALITY FROM LEUKEMIA IN WORKERS EXPOSED TO ELECTRICAL AND MAGNETIC FIELDS (Correspondence)
New England J. Med., Vol. 304, p. 249 (1982) (III-53)

86
Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981) (III-31)

58
Olsen, R.G. and W.C. Hammer
THERMOGRAPHIC ANALYSIS OF WAVEGUIDE-IRRADIATED INSECT PUPAE
In Abstracts of Open Symposium on the Biological Effects of Electromagnetic Waves, Helsinki, Finland, p. 62 (1978) (II-50)

35
Oscar, K.J. and T.D. Hawkins
MICROWAVE ALTERATION OF THE BLOOD-BRAIN BARRIER SYSTEM OF RATS
Brain Res., Vol. 126, pp. 281-293 (1977) (I-112)

36
Oscar, K.J., S.P. Gruenau, M.T. Folker, and S.I. Rapoport
LOCAL CEREBRAL BLOOD FLOW AFTER MICROWAVE EXPOSURE
Brain Res., Vol. 204, No. 1, pp. 220-225 (1981) (I-115)

16
Pay, T.L., E.C. Beyer, and C.F. Reichelderfer
MICROWAVE EFFECTS ON REPRODUCTIVE CAPACITY AND GENETIC TRANSMISSION IN DROSOPHILA MELANOGASTER
J. Microwave Power, Vol. 7, No.2, pp. 75-82 (1972) (I-61)

6
Pazderova, J.
WORKERS' STATE OF HEALTH UNDER LONG-TERM EXPOSURE TO ELECTROMAGNETIC RADIATION IN THE VHF BAND (30-300 MHz)
Pracovni Lekarstvi (in Czech), Vol. 23, No. 8, pp. 265-271 (1971).
English translation: JPRS No. UDC 616-001.228.1-057-07 (1971) (I-38)

7
Pazderova, J., J. Pickova, and V. Bryndova
BLOOD PROTEINS IN PERSONNEL OF TELEVISION AND RADIO TRANSMITTING STATIONS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 281-288 (1974) (I-40)

8
Peacock, P.B., J.W. Simpson, C.A. Alford, Jr., and F. Saunders
CONGENITAL ANOMALIES IN ALABAMA
J. Med. Assoc. Ala., Vol. 41, No. 1, pp. 42-50 (1971) (I-42)

59
Pickard, W.F. and R.G. Olsen
DEVELOPMENTAL EFFECTS OF MICROWAVES ON TENEBRIO: INFLUENCES OF CULTURING PROTOCOL AND OF CARRIER FREQUENCY
Radio Sci., Vol. 14, No. 6S, pp. 181-185 (1979) (II-52)

110
Preston, E., E.J. Vavasour, and H.M. Assenheim
PERMEABILITY OF THE BLOOD-BRAIN BARRIER TO MANNITOL IN THE RAT FOLLOWING 2450 MHZ MICROWAVE IRRADIATION
Brain Res., Vol. 174, pp. 109-117 (1979) (III-130)

37
Rapoport, S.I., K. Ohno, W.R. Fredericks, and K.D. Pettigrew
A QUANTITATIVE METHOD FOR MEASURING ALTERED CEREBROVASCULAR PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 345-348 (1979) (I-117)

9
Robinette, C.D. and C. Silverman
CAUSES OF DEATH FOLLOWING OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR) 1950-1974
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIOFREQUENCY/MICROWAVES, Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication No. (FDA) 77-8026 (1977) (I-44)

60
Rugh, R., E.I. Ginns, H.S. Ho, and W.M. Leach
RESPONSES OF THE MOUSE TO MICROWAVE RADIATION DURING ESTROUS CYCLE AND PREGNANCY
Radiat. Res., Vol. 62, pp. 225-241 (1975) (II-56)

49
Rukspollmuang, S. and K.-M. Chen
HEATING OF SPHERICAL VERSUS REALISTIC MODELS OF HUMAN AND INFRAHUMAN HEADS BY ELECTROMAGNETIC WAVES
Radio Sci., Vol. 14, No. 6S, pp. 51-62 (1979) (I-161)

10
Sadchikova, M.N.
CLINICAL MANIFESTATIONS OF REACTIONS TO MICROWAVE IRRADIATION IN VARIOUS OCCUPATIONAL GROUPS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 261-267 (1974) (I-47)

96
Schlagel, C.J., K. Sulek, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE. II. STUDIES ON THE MECHANISMS CONTROLLING SUSCEPTIBILITY TO MICROWAVE-INDUCED INCREASES IN COMPLEMENT RECEPTOR-POSITIVE SPLEEN CELLS
Bioelectromagnetics, Vol. 1, No. 4, pp. 405-414 (1980) (III-68)

117
Schrot, J., J.R. Thomas, and R.A. Banvard
MODIFICATION OF THE REPEATED ACQUISITION OF RESPONSE SEQUENCES IN RATS BY LOW-LEVEL MICROWAVE EXPOSURE
Bioelectromagnetics, Vol. 1, No. 1, pp. 89-99 (1980) (III-156)

42
Sheppard, A.R., S.M. Bawin, and W.R. Adey
MODELS OF LONG-RANGE ORDER IN CEREBRAL MACROMOLECULES: EFFECTS OF SUB-ELF AND OF MODULATED VHF AND UHF FIELDS
Radio Sci., Vol. 14, No. 6S, pp. 141-145 (1979) (I-133)

11
Siekierzynski, M.
A STUDY OF THE HEALTH STATUS OF MICROWAVE WORKERS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 273-280 (1974) (I-49)

12
Sigler, A.T., A.M. Lilienfeld, B.H. Cohen, and J.E. Westlake
RADIATION EXPOSURE IN PARENTS OF CHILDREN WITH MONGOLISM (DOWN'S SYNDROME)
Bull. Johns Hopkins Hosp., Vol. 117, pp. 374-395 (1965) (I-51)

108
Smialowicz, R.J., J.S. Ali, E. Berman, S.J. Bursian, J.B. Kinn, C.G. Liddle, L.W. Reiter, and C.M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b) (III-121)

95
Smialowicz, R.J., P.L. Brugnolotti, and M.M. Riddle
COMPLEMENT RECEPTOR POSITIVE SPLEEN CELLS IN MICROWAVE (2450-MHZ)-IRRADIATED MICE
J. Microwave Power, Vol. 16, No. 1, pp. 73-77 (1981c) (III-64)

75
Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a) (II-114)

94
Smialowicz, R.J., M.M. Riddle, R.R. Rogers, and G.A. Stott
ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 121-126 (1982b) (III-59)

93
Smialowicz, R.J., M.M. Riddle, C.M. Weil, P.L. Brugnolotti, and J.B. Kinn
ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHZ RADIO FREQUENCY RADIATION (Brief Communication)
Bioelectromagnetics, Vol. 3, No. 4, pp. 467-470 (1982c) (III-56)

106
Smialowicz, R.J., C.M. Weil, J.B. Kinn, and J.A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a) (III-112)

107
Smialowicz, R.J., C.M. Weil, P. Marsh, M.M. Riddle, R.R. Rogers, and B.F. Rehnberg
BIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE OF RATS TO 970-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 2, No. 3, pp. 279-284 (1981d) (III-117)

38
Spackman, D.H., V. Riley, A.W. Guy, and C.-K. Chou
STUDIES OF RF RADIATION EFFECTS ON BLOOD-BRAIN BARRIER PERMEABILITY USING FLUORESCEIN AND AMINO ACIDS
Presented at the Open Symposium on Biological Effects of Electromagnetic Waves, Helsinki, Finland, 1-8 August 1978 (I-119)

61
Stavinoha, W.B., A. Modak, M.A. Medina, and A.E. Gass
GROWTH AND DEVELOPMENT OF NEONATAL MICE EXPOSED TO HIGH-FREQUENCY ELECTROMAGNETIC WAVES
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report SAM-TR-75-51 on Contract F41609-74-C-0018, submitted by University of Texas Health Science Center, San Antonio, Texas (1975) (II-60)

63
Stern, S., L. Margolin, B. Weiss, S.-T. Lu, and S.M. Michaelson
MICROWAVES: EFFECT ON THERMOREGULATORY BEHAVIOR IN RATS
Science, Vol. 206, pp. 1198-1201 (7 December 1979) (II-75)

76
Stodolnik-Baranska, W.
THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 189-195 (1974) (II-117)

101
Sulek, K., C.J. Schlagel, W. Wiktor-Jedrzejczak, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980) (III-90)

112
Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979) (III-137)

104
Szmigielski, S., W. Roszkowski, M. Kobus, and J. Jeljaszewicz
MODIFICATION OF EXPERIMENTAL ACUTE STAPHYLOCOCCAL INFECTIONS BY LONG-TERM EXPOSITION TO NON-THERMAL MICROWAVES OR WHOLE BODY MICROWAVE HYPERTHERMIA
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 127-132 (June-July 1980) (III-103)

118
Takashima, S., B. Onaral, and H.P. Schwan
EFFECTS OF MODULATED RF ENERGY ON THE EEG OF MAMMALIAN BRAINS
Rad. and Environm. Biophys., Vol. 16, pp. 15-27 (1979) (III-160)

65
Thomas, J.R., L.S. Burch, and S.S. Yeandle
MICROWAVE RADIATION AND CHLORDIAZEPOXIDE: SYNERGISTIC EFFECTS ON FIXED-INTERVAL BEHAVIOR
Science, Vol. 203, pp. 1357-1358 (1979) (II-80)

64
Thomas, J.R., J. Schrot, and R.A. Banvard
BEHAVIORAL EFFECTS OF CHLORPROMAZINE AND DIAZEPAM COMBINED WITH LOW-LEVEL MICROWAVES
Neurobehav. Toxicol., Vol. 2, pp. 131-135 (1980) (II-77)

17
Varma, M.M. and E.A. Traboulay, Jr.
EVALUATION OF DOMINANT LETHAL TEST AND DNA STUDIES IN MEASURING MUTAGENICITY CAUSED BY NON-IONIZING RADIATION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW publication (FDA) 77-8010, pp. 386-396 (1976) (I-63)

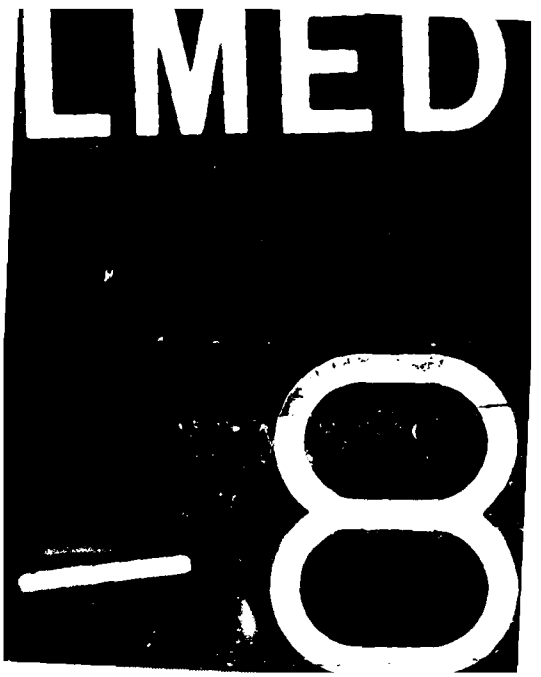
18
Varma, M.M., E.L. Dage, and S.R. Joshi
MUTAGENICITY INDUCED BY NON-IONIZING RADIATION IN SWISS MALE MICE
In C.C. Johnson and M. Shore (eds.). BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 397-405 (1976) (I-65)

114
Ward, T.R., J.A. Elder, M.D. Long, and D. Svendsgaard
MEASUREMENT OF BLOOD-BRAIN BARRIER PERMEATION IN RATS DURING EXPOSURE TO 2450-MHZ MICROWAVES
Bioelectromagnetics, Vol. 3, No. 3, pp. 371-383 (1982) (III-145)

31
White, R.M.
GENERATION OF ELASTIC WAVES BY TRANSIENT SURFACE HEATING
J. Appl. Phys., Vol. 34, No. 12, pp. 3559-3567 (1963) (I-100)

77
Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
EFFECT OF MICROWAVES (2450-MHZ) ON THE IMMUNE SYSTEM IN MICE: STUDIES OF NUCLEIC ACID AND PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 1, No. 2, pp. 161-170 (1980) (II-119)

78
Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977) (II-122)


LMED
8